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EDITORIAL

RABIES

An article in this issue of *The British Veterinary Journal* concerns a disease which, as far as is known, may affect all warm-blooded animals. It has been recognised from the most ancient times and the signs and symptoms it evokes strike terror in the heart of man. It would appear to be a disease which has retained throughout the centuries a constant form or type and a virulence of high degree and the descriptions of its signs and symptoms as given by the ancient Greek physicians are the same as those which are manifested to-day. Aristotle, writing in the fourth century B.C., said: "Dogs suffer from madness which puts them in a state of fury and all the animals that they bite, when in this condition, become also attacked by rabies." The natural reservoir of infection is in those animals which use their teeth as a means of attack, and the wild carnivora are the prime propagators of the disease. Certain blood-sucking bats are implicated also but to a lesser degree. As the causal virus cannot persist and propagate outside the animal body the disease must undergo some modification in its natural reservoir. Some of its hosts must develop a degree of immunity from its immediate effect and in consequence assume the role of carriers otherwise the wild carnivora would be extinct. The disease has a world-wide distribution and it has been reported in most of those countries which naturally harbour carnivores. It has been kept out of other countries, in which

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it was not naturally indigenous by quarantine measures. The causal agent is a neurotrophic virus and until Pasteur evolved his vaccine in 1885 and saved the life of Joseph Meister, any man or susceptible animal inoculated with the virus was doomed to die a horrible death. All bites from known rabid dogs do not necessarily have fatal consequence. The saliva may or may not contain the lethal poison but the percentage of those who have suffered after being bitten by a known rabid animal is so high that even an animal which is only under suspicion can cause terror in a community.

Pasteur's vaccine brought salvation to man for although the period of incubation in naturally-infected cases cannot be estimated precisely, if the treatment be applied at or shortly after the incident, calamity can be averted. It appeared that a complete answer had been found. Clinics were opened in many countries where the treatment could be applied. Some years after the dark cloud had been lifted and people had time to think, some doubt was cast upon the real value of the method as estimated from the apparent wonderful protection that was afforded to all those who were thought to have been subjected to risk. There is no doubt that many people who have been treated were not infected and they were never in any danger other than that which can be ascribed to psychological causes. In many cases positive proof that the dog was rabid was lacking and also if the dog was positive it was not known for certain if the saliva had contained the virus. The only way to solve these doubts would be to omit to provide treatment, and such a practice would be untenable.

In recent years research workers have sought for a means of prophylaxis. A vaccine and a hyperimmune serum have been evolved and in August, 1954, they were put to a most severe practical test. The details of this test are reported by M. Baltazad and M. Bahmanyar in *Bull. World Hlth. Org.*, 1955, *13*, 747. A rabid wolf attacked a number of people in a Persian village. A dog and six cows were victims also. The reign of terror lasted for several hours before the wolf was killed. Eleven people bitten on the trunks and limbs all recovered. Some were given serum and vaccine, others only vaccine. Eighteen victims had head wounds. Five of these were given vaccine only and three died. Thirteen were given serum also and only one died; he was given only one dose of the serum. Five were given serum on the first and fifth days and all recovered. The remaining patient, a boy, had severe head injuries, including tearing of the dura mata, and he exhibited signs of meningitis when presented for treatment. He was given six doses of serum and a course of vaccine, the treatment being spread over three weeks. He was given penicillin also. He recovered. This unfortunate incident yet fortuitous clinical trial has done much to support the therapeutic value of both vaccine and serum.

It is good to know that such valuable aids in treatment have been evolved, but the rational way to attack and abolish this dread disease is to eliminate it by destroying it in its reservoir and by protecting those who are subject to risk by vaccination or other means. The work that has been done in this field by our contributors and their colleagues in Malaya gives a lead to the world.

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GENERAL ARTICLES

I. A SUMMARY OF THE 1952-1954 RABIES CONTROL CAMPAIGN IN MALAYA

with particular reference to the use of Chicken-Embryo Vaccine before and after Eradication has been effected

By C. W. WELLS, O.B.E., B.Sc., M.R.C.V.S., D.T.V.M.
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II. FORECASTING THE PROPORTION OF VACCINATED ANIMALS

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Part I.

A RABIES control campaign involving the mass vaccination of dogs was conducted in the Federation of Malaya from August, 1952, to December, 1954, by the end of which period it was clear that eradication of the disease had been effected. Interim descriptions of the early stages of the campaign have been published (Wells, 1953, 1954, 1954*a*; World Health Organisation, 1954). The present paper summarises these earlier reports, which cover the period from August, 1952, to November, 1953, and includes data for the period from December, 1953, to July, 1955. The statistical appendix which forms the second half of the paper shows that after a campaign in which eradication of rabies was achieved the density of the immune-dog population decreases at a rapid rate if vaccination ceases to be a routine, even when the elimination of stray dogs is maintained at a relatively high level.

The Malayan authorities believe that chicken-embryo vaccine (Flury strain)* was the main factor in effecting eradication. They are, however, for reasons which are discussed, unable to take full advantage of the long period of immunity that it confers. Conclusions in respect of this vaccine under Malayan conditions may, therefore, be of interest, particularly in view of a recent recommendation that in certain circumstances its triennial exhibition will provide adequate protection in areas threatened with the introduction of rabies (World Health Organisation, 1954), a recommendation that cannot be adopted in Malaya unless other measures, impracticable on the grounds of expense, are introduced simultaneously.

The principal features of the campaign in each of the years from 1952 to 1955 are described below.

1952.

Rabies had been endemic in the northern part of Malaya for not less than 30 years before the fulminating extension of the disease in early 1952. Although,

* Lederle Laboratories Division, American Cyanamid Company, New York.

before the second World War, small localised outbreaks had been controlled as they occurred, much concern was caused by the high post-war average of 112 confirmed canine cases a year, despite strong legislation, a vaccination service and stray dog destruction. The spread of the disease southwards to Kuala Lumpur, the Federal capital, in April, 1952, after 20 years without a rabies epidemic, created very rapidly a most serious situation. The town contained about 22,000 dogs, many of which were ownerless.

Further spread down the peninsula to other States was feared and an intensive attack on a large scale was planned; the most seriously affected areas and the available supplies of vaccine were the limiting factors.

In August-December, 1952, attention was concentrated on five heavily infected areas, i.e., Kuala Lumpur and its suburbs in the State of Selangor, and four areas in an adjoining State (Perak) in which the incidence of the disease had been high for several years. Chicken-embryo vaccine was used in Kuala Lumpur, and a Semple-type nervous-tissue vaccine and a small quantity (150 doses) of chicken-embryo vaccine in the other four areas; sufficient chicken-embryo vaccine for general use was not available at the time.

A muzzling order was enforced, not because the authorities placed any marked reliance on it as an anti-rabies measure *per se,* but because it helped considerably to distinguish the presumably ownerless dog from one whose owner was obeying the law. The muzzling order was rescinded in all areas one month after it had been estimated that not less than 75 per cent of the dog population in each area had been vaccinated. This concession did much to popularise the vaccination campaign.

The movement of dogs from rabies-infected areas to rabies-free ones was prohibited except under certain specific conditions of vaccination, ear-tattooing and quarantine (Gordon Smith and Wells, 1955).

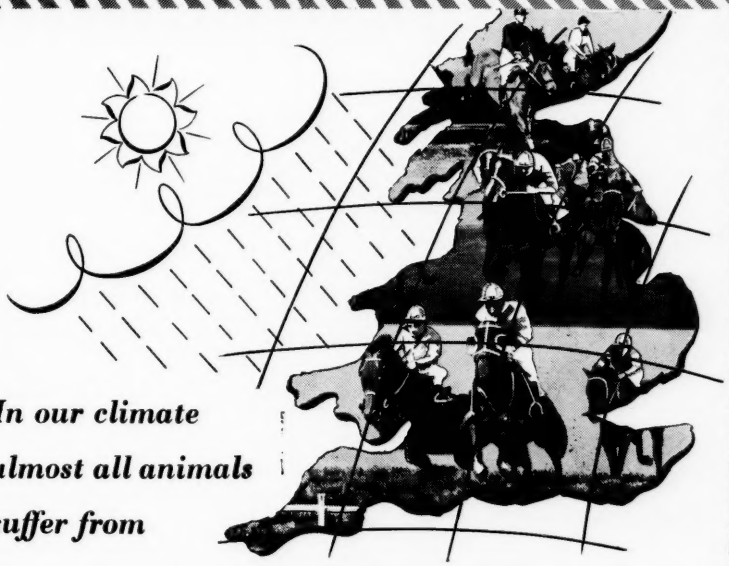
18,067 dogs over 4 months of age (i.e., 17,917 in Selangor and 150 in Perak) were compulsorily vaccinated with the chicken-embryo vaccine, and 12,052 with the Semple-type vaccine. An additional 1,100 dogs had been presented for voluntary vaccination with the latter vaccine before the commencement of the compulsory vaccination campaign in August. 10,300 dogs not presented for vaccination in the five areas were destroyed. The subsequent fall in incidence is shown in Table I.

TABLE I

The fall in incidence of canine rabies in five heavily infected areas during 1952, after compulsory vaccination.

Locality	Confirmed canine cases 1952												Total vaccinations	
	Jan	Feb	Mar	Apr	May	Jun	Jly	Aug*	Sep	Oct	Nov	Dec	Jan-Jly	Aug-Dec
Kuala Lumpur	nil	nil	nil	7	13	12	33	24	11	3	2	nil	nil	17,917
Four areas in adjoining State	5	15	3	11	3	3	1	13	9	6	3	1	1,100	12,202
Totals:	5	15	3	18	16	15	34	37	20	9	5	1	1,100	30,119

* Vaccinations commenced simultaneously in all areas in August.



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Notes: (i) In Kuala Lumpur, seven cases (chicken-embryo vaccine) occurred 7 to 20 days after vaccination. (ii) In the other four areas, six cases (Semple-type vaccine) occurred 14 to 81 days after vaccination. (iii) The remaining cases were in *unvaccinated* dogs.

The total of over 30,000 vaccinated dogs is estimated to have been not less than 75 per cent of the dog population in each of the five areas.

Vaccinated dogs were distinguished by an easily recognised tag hung from the collar. (The shape, colour and size of the tags used in 1952, 1953 and 1954 differed materially. Size was considered an important factor, to make recognition easy for the dog-shooters, particularly at night. The tags were made large—purposely so.)

198 confirmed canine cases were recorded in Malaya during 1952. The many clinical cases of rabies destroyed by dog-shooting teams, but not submitted for laboratory confirmation, are *not* included in this total.

1953.

By the end of 1952 adequate stocks of chicken-embryo vaccine for an extension of the campaign had been accumulated. The second phase was to enforce compulsory vaccination in all rabies-infected States and in certain threatened areas adjoining them. The plan was to vaccinate, as the first step, all dogs in a belt running east and west about the middle of the block of the rabies-infected and rabies-threatened States, having first created an immune strip to the south of Kuala Lumpur. All teams concentrated in the central belt and, as soon as vaccinations in it were completed, turned north and south and vaccinated to the limits of the block. In this way a gradually widening belt was established rapidly which limited the chances of infiltration of the disease from the infected northern to the susceptible southern half of the country.

All dogs four months of age and above were required to be vaccinated, regardless of whether they had been vaccinated in 1952. Chicken-embryo vaccine only was used at this time. The decline in incidence continued, as is shown in Table II.

TABLE II

The decline in incidence of canine rabies during 1953, after compulsory vaccination in all rabies-infected States.

Locality	Confirmed canine cases 1953												Total vaccinations
	Jan*	Feb	Mar	Apr	May	Jun	Jly	Aug	Sep	Oct	Nov	Dec	
All rabies-infected States	1	6	5	1	1	1	nil	nil	nil	nil	nil	nil	73,694

* Vaccinations commenced simultaneously in January.

Notes: (i) The one case in January was vaccinated nine days previously with chicken-embryo vaccine. (ii) The remaining 14 cases were *unvaccinated* dogs.

During the year, 46,288 stray dogs were destroyed in the Federation. The total of nearly 73,700 vaccinated dogs is estimated to have been about 60 per

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cent of the total dog population of the Federation in 1953, and not less than 80 per cent of the dog population in each of the rabies-infected States.

1954.

Since it was evident by the middle of 1953 that spread had been controlled, hope was entertained that actual eradication might be accomplished. As already described, dogs in rabies-infected States and certain adjoining belts only had been vaccinated during 1952 and 1953. To have assumed that no movement of dogs had occurred to the unprotected, rabies-free States in the south and east would, however, have been dangerous. The third phase was, therefore, a *pan-Federation,* compulsory mass-vaccination campaign.

By vaccinating dogs three months of age and above in every State and Settlement of the Federation, disregarding all previous vaccination histories, and by coupling with this an intensive elimination of dogs unvaccinated by a certain date, the percentage of immune dogs in the country could, it was believed, be raised to a level where any outbreaks during at least the following 12 months would be self-limiting.

The stringent legislation that supported the two earlier phases was maintained, including the possibly unique provision, operated under proper safeguards, that private houses could be searched for unvaccinated dogs. The penalties for harbouring an unvaccinated dog were very severe, with the result that evasion, after a few salutary examples of official determination to enforce the law, ceased abruptly.

All available personnel were concentrated on the mass-vaccination drive in order to complete the task within 10 weeks from the opening date on January 2. This period may appear unduly long, but journeys by road, village track and river to isolated areas, and the scattered human population in many others, made it impossible to complete the programme in less time. In the larger towns vaccination was completed in 14-21 days.

115,076 dogs were vaccinated with chicken-embryo vaccine during the year, and 30,020 strays are known to have been destroyed, but thousands were disposed of by owners to whom the keeping of a dog had become more of a liability than an asset. One reason for this was that the re-grouping of peasants in some areas into more compact communities, made necessary by the state of civil emergency in the country, meant that a watch-dog was less essential. For another, many owners in the non-infected States realised for the first time that the possession of a dog implied a certain financial obligation, one that a large number had successfully avoided for several years.

Again, during 1954, no consideration was given to a dog's previous vaccination history. It is estimated that, at the end of the year, not less than 85 per cent of the dog population of the country had been vaccinated. This percentage varied from not less than 75 per cent in any given area to as high as 95 per cent in the towns. The thoroughness with which State vaccination teams conducted their programmes eliminated any chances of " patchiness " occurring in the distribution of the immunised population.

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One case only of animal rabies was recorded in 1954. This occurred in March in a goat in an isolated Malayan village on the Thailand-Malaya border. It is highly probable that infection was introduced by a rabid dog from across the border, where the disease is prevalent and where no rabies-control measures are at present taken.

1955.

During the current year, a cordon of immune dogs (the "immune belt") is being maintained along the Malayan side of the Malaya-Thailand border, and the elimination of unvaccinated dogs has a high priority. As in 1953 and 1954, dogs imported into Malaya from rabies-infected countries are vaccinated with chicken-embryo vaccine on arrival, ear-tattooed, and quarantined for 30 days at the port of entry. Dogs from rabies-free countries are admitted without quarantine, subject to the production of certain certificates.

Discussion

The division of the control programme into three phases was dictated as much by the availability of personnel, materials, and money in the early stages as it was by the desirability of giving the operators time to develop a routine before embarking on the more ambitious phase of compulsory vaccination throughout the whole of the Federation. During August-December, 1952, officers from non-infected States were posted to static and mobile vaccination teams for a period to give them practical experience of the procedure.

Contrary to the W.H.O. recommendation that vaccination should be free (World Health Organisation, 1954), a charge was levied. This served the double purpose of paying, to a considerable extent, for the cost of the campaign, and of bringing into the open a very large number of dogs whose owners were not prepared to pay the fee: as already mentioned, the penalty for harbouring an unvaccinated dog was a severe one. The official view was that if an owner kept a dog he must accept certain responsibilities with regard to it: to license it annually was one requirement. During the second and third phases of the campaign licensing and vaccination was made a combined operation at a fee of $5 (Malayan). ($1 Malaya = 2s. 4d. sterling = 33 cents U.S.)

When, during late 1954, it appeared that eradication had been effected, consideration was given to pan-Federation compulsory vaccination as an annual routine, but was abandoned. The Federation of Malaya, a peninsula with a narrow land frontier, lends itself to a comparatively easily-maintained state of freedom from exotic diseases. Although Singapore island is administered by a separate Government, the disease control regulations operated by the two territories are, for all practical purposes, identical. Control is rigid at sea and air ports and it is on the maintenance of this control and on the solidity of the "immune belt" along the land frontier that the Federation's future freedom from rabies will depend. Again, to maintain an annual, pan-Federation, compulsory vaccination service would be expensive; it would be difficult to persuade the public of its necessity in the absence of outbreaks, and the relatively

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long period of immunity conferred by chicken-embryo vaccine would not be utilised.

A simple scheme of control was devised and was introduced in January, 1955: only time and experience will determine whether it is adequate for Malayan conditions or whether periodical mass vaccination will have to be superimposed. It has three characteristics:

(*i*) The maintenance of the "immune belt," 30 to 50 miles wide on the Malayan side of the Thailand-Malaya border, by the compulsory annual vaccination within it of all dogs three months of age and above;

(*ii*) A relentless reduction of stray dogs throughout the whole of the country; and

(*iii*) The employment of "blitz" tactics to suppress any future foci of infection. The Malayan authorities feel confident that with the experience they have gained during the past three years in the operation of mobile vaccination units, it would be possible to cordon off any infected area and to vaccinate in a very short time not less than 80 per cent of the dogs within a radius of 20 to 30 miles of the centre of the epidemic. The speed with which the operation could be completed would, of course, depend on whether an urban or rural district were affected, but to deal with an area of the size quoted would probably never take more than a week, and perhaps considerably less. (The W.H.O. Expert Committee on Rabies (World Health Organisation, 1954) states that "the swift reduction of susceptible animals . . . can be achieved by the immunisation of at least 70 per cent of the entire dog population of the area in the shortest possible period.") A stock of chicken-embryo vaccine is held for emergency use. Teams of dog-shooters would tour the area immediately in the wake of the vaccination teams and would deal summarily with any dogs not wearing the special vaccination tag. These methods proved to be very satisfactory in practice during 1952 and 1953.

Observed Advantages of Chicken-Embryo Vaccine.

A number of advantages of chicken-embryo vaccine over the Semple-type nervous-tissue vaccine used previously in Malaya have been apparent.

Firstly, there was strong experimental evidence available in 1952 that chicken-embryo vaccine conferred a solid immunity for at least one year with a single intramuscular injection (Koprowski and Black, 1952). Previous Malayan experience with Semple-type vaccine had shown that at least two injections, at an interval of six months, would be required to confer the same protection. The use of chicken-embryo vaccine, therefore, enabled the authorities to proceed confidently, without having to "look over their shoulders" continually for breakdowns (Wells, 1954*a*).

Secondly, early Malayan field data suggested that at the height of a serious epidemic the use of chicken-embryo vaccine either blocked development of the disease in some exposed dogs (Wells, 1954*a*) or, possibly, accelerated its development in others.

Thirdly, in contrast with experience with Semple-type vaccine, no cases of post-vaccinal paralysis or of encephalomyelitis have been recorded in over 211,000 dogs vaccinated with chicken-embryo vaccine to date (October, 1955). Rabies consciousness in the general public was high at the time the bulk of the vaccinations were performed; the reporting system was efficient; and they were not few who might have asserted, had post-vaccinal paralyses occurred, that in that respect chicken-embryo vaccine showed no advantage over the Semple-type vaccine. That no reports of paralysis were made is not proof that unrecorded cases did not occur: however, if they did occur they must have been very rare indeed. It is difficult, therefore, to reconcile with these Malayan findings those cited in a recent paper (Foley, 1955) where, " out of 870 selected, apparently healthy dogs " vaccinated with " chick-embryo cultured rabies vaccine " there were nine cases of post-vaccinal paralysis, of which four died from causes not specified but presumably attributed directly to the vaccine. In the absence of much more detailed protocols of the vaccinations and the vaccine used it is not possible to comment beyond saying that in Malaya, on a scale of vaccination over 240 times as large as that reported by Foley, nothing even remotely approaching the unfavourable sequelæ he cites were recorded. The eight deaths from rabies within 20 days of vaccination with chicken-embryo vaccine (Flury strain) have been mentioned in connection with the 1952 and 1953 programmes in Malaya: it is not improbable that all were in the incubative stage of the disease when vaccinated.

The problems associated, in the tropics, with handling a comparatively fragile product such as chicken-embryo vaccine—which, being a live vaccine, and having a limited period of potency, needs special care—were solved with little real difficulty. The details of transport of the vaccine have been described elsewhere (Gordon Smith and Wells, 1955).

Triennial Vaccination of Dogs with Chicken-Embryo Vaccine.

In its Second Report (World Health Organisation, 1954) the W.H.O. Expert Committee on Rabies makes the following recommendation:—

> " In rabies-free areas faced by the constant danger of introduction of the disease, continued programmes of vaccination should be adopted which would provide for revaccination of dogs every three years with chicken-embryo vaccine or for annual revaccination with nervous-tissue vaccines."

It is felt that some authorities, seeking a short cut to rabies eradication or to the maintenance of a rabies-free state, might accept this recommendation uncritically, and in a sense scarcely intended by the Committee, and assume that a mass vaccination campaign using chicken-embryo vaccine once every three years would solve their problems.*

* The writers feel that "a continuous, long-term programme" would be less liable to misinterpretation than "continued programmes." What the Expert Committee certainly intends is that every dog over three months of age in the community should be vaccinated with chicken-embryo vaccine once in three years in a programme that is continuous not only throughout the course of any one year, but throughout a number of years in an unbroken series. The length of the series would depend on individual circumstances. This interpretation has been confirmed by correspondence with the Secretary of the Expert Committee.

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To enforce mass vaccination once only every three years would result in a rapid decrease in the proportion of immune dogs in the population in the interim, even if the elimination of unvaccinated dogs could be made a selective process and if it were maintained at a high rate. As is shown in the second part of the paper, to prevent an initial 90 per cent immunised proportion of the population falling below 70 per cent in three years it would be necessary to shoot 40,000 *unvaccinated* dogs per year in the Federation of Malaya.

The related proposal (World Health Organisation, 1954) that " Dogs which have been vaccinated . . . when under six months of age should be revaccinated within the first year of life," would again be very expensive. Although this is done in the " immune belt " its general application throughout the Federation would be impossible.

If the three years period of immunity conferred by this vaccine were to be utilised in a control programme the permanent marking of every dog would appear to be essential. Ear-tattooing is the most obvious method, but is resented by the majority of owners. The delay which the operation entails in an intensive programme might severely limit its use, but the alternative of registering vaccinated dogs appears to be of doubtful value during a mass vaccination campaign.

Strong representations were made by the public in Malaya for the registration of vaccinated dogs, but were successfully opposed on the following grounds :—

(*i*) To have identified every dog *beyond reasonable doubt* would have been virtually impossible. Any attempt to have done so would have slowed down the vaccination procedure to an impractical degree.

(*ii*) Public pressure to issue replacement vaccination tags for those alleged to have been " lost " would have been strong. The abuse to which such a concession would have been put needs no stressing.

(*iii*) It was essential that the public should be made to realise that the loss of a vaccination tag involved immediate re-presentation of the dog for vaccination, since any dog without a tag would be regarded as unvaccinated and would be summarily destroyed. Furthermore, its owner, if traced, would be liable to a heavy fine.

(*iv*) Under Malayan conditions annual dog registration (i.e., " licensing ") had already proved to be of very doubtful value. Addresses of owners were frequently vague, particularly in the areas potentially most dangerous from the rabies point of view, i.e., the crowded and built-up parts of the towns. Most licensing authorities charged a lower fee for male dogs than for bitches, and written receipts for licence fees were issued. It is known that many bitches were licensed as males because production of the dog at the time of licensing was not required. When a licence tag was lost a replacement could be obtained for a purely nominal fee on production of the original receipt. Because no limit was set on the number of " lost " licence tags an owner was permitted, written registration had been reduced to a farce.

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(*v*) Because this " replacement " system had become so ingrained in the dog-owning public prior to the introduction of mass vaccination, only a clean break with it could have avoided compromising the rabies-control programme. Had replacement *vaccination* tags been issued in the same way as replacement *licence* tags, the number of dogs vaccinated would have been considerably less than was actually the case.

It was difficult to see, therefore, how the Committee's recommendation could be adopted unless, before the current year's vaccination tag was issued, *all* dogs were produced for inspection, and vaccinated if not already ear-tattooed. By accepting a written registration of vaccination instead of demanding the annual production of the dog, control authorities might, in a triennial vaccination campaign, seriously compromise their programmes. In Malaya, ear-tattooing was abandoned after a small-scale trial. The majority of Malayan dogs are not notable for their tractability with either their owners or strangers, so that tattooing would have caused a mêlée in each vaccination centre instead of the orderly and rapid procession that was, in fact, achieved. Ear-tattooing is, however, compulsory for dogs imported from rabies-infected countries, and its introduction in the immune belt along the Thailand-Malaya border is being considered.

To the extent that the last recorded case of human or canine rabies in Malaya was in a dog in June, 1953, i.e., 28 months ago at the time this paper was prepared, and that the only other subsequent recorded case, in a goat in March, 1954, is considered to be of extraneous origin, the 1952-54 control campaign in the Federation of Malaya can be said to have been successful and eradication to have been effected.

Public co-operation was excellent throughout; many owners would, in fact, have welcomed vaccination as an annual routine. Confidence in the vaccine was rapidly established, particularly in those States whose experience of the Semple-type of vaccine stretched back over many years.

The campaign was conducted on the broad lines that the best results would be achieved by giving continuous publicity to it through every available medium, by an uncompromising application of strong legislation that left few loopholes for evasion, and by carrying the campaign through " with a syringe in one hand and a gun in the other."

Summary

Rabies had been endemic in the northern part of Malaya for not less than 30 years prior to the serious extension to the south that occurred in early 1952. Earlier attempts to control outbreaks by legislation, stray dog destruction, and the use of a Semple-type vaccine had had limited success only. A country-wide, compulsory, mass vaccination programme was carried out between August, 1952, and December, 1954, the principal features of which are described. From an annual average of 112 confirmed positive canine cases for the years 1947-1951, and a total of 198 in 1952, the incidence dropped to a total of 15 for the first six months of 1953. No case in a dog has been reported since June, 1953. This reduction is attributed to the use of chicken-embryo vaccine (Flury strain)

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and to the enforcement of stringent legislation. Some advantages of chicken-embryo vaccine over Semple-type vaccine used previously in Malaya have been apparent. A recent W.H.O. recommendation concerning triennial vaccination with the vaccine is considered to be impracticable in Malaya, and reasons for its non-adoption are discussed.

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II. FORECASTING THE PROPORTION OF VACCINATED ANIMALS

Part II.

Introduction

1. Suppose that the proportion of vaccinated animals in the dog population is known at some given instant and we wish to estimate the changes which this proportion is likely to undergo during the next t years if no further vaccinations are performed. In practice this vaccinated proportion will be subjected to irregular changes as a result of births and deaths, including deaths from shooting in a planned anti-rabies campaign; the possibility of animals vaccinated with chicken-embryo adapted vaccine (Flury strain) losing their immunity is precluded by restricting the period covered by the forecast to three years. A precise forecast of the changes in the vaccinated proportion is beyond the scope of this appendix, but a theoretical model is described which provides a rough approximation.

Theoretical model.

2. The first major assumption is that the proportion of bitches in the total population remains effectively unchanged throughout the period of t years, irrespective of changes in the size of the population. The present proportion of bitches in the population in Malaya is roughly estimated as 1/6, and this inequality in the numbers of dogs and bitches is mainly due to their owners destroying the female members of a litter shortly after birth. It seems unlikely that this practice will be unduly affected by other population changes, and it is also reasonable to stipulate that in any planned shooting campaign there would be no sex discrimination which would cause large changes in the proportion of bitches.

3. Consider first the changes in the population total. Let p = the proportion of adult bitches in the total population, and b = the average number of viable pups produced annually per adult bitch.

If the period of t years is divided into m small intervals each of duration t/m years, then

Npbt/m = average number of animals produced during a small interval t/m years,

where N is approximately* equal to the total number of animals at the beginning of such an interval.

4. If y years be the average expectation of life of an animal surviving birth (and the destruction of members of litters shortly after birth), then the average number of such animals dying during a small interval t/m years is approximately Nt/my.

5. Various hypothetical shooting schemes might be defined, but the simple case where a constant number of animals, D, are shot annually throughout the period of t years is first examined. The shooting is assumed to be at a steady rate, so that in any short interval of t/m years, the number shot will be Dt/m.

6. Consider now the discrete changes in the size of the total population after each small time interval.

Let N_o = total number of animals at time o.
$N_{t/m}$ = total number of animals at time t/m.
$N_{2t/m}$ = total number of animals at time 2t/m.
and,
$N_{mt/m} = N_t$ = total number of animals at time t years.

The number of animals at the end of any interval = the number of animals at the beginning of the interval, plus the number of births during the interval, minus the number of deaths (" normal " and shooting) during the interval.

Hence :

$$N_{t/m} = N_o + N_o\frac{tbp}{m} - N_o\frac{t}{my} - \frac{Dt}{m}$$

$$N_{2t/m} = N_{t/m} + N_{t/m} \cdot \frac{tbp}{m} - N_{t/m} \cdot \frac{t}{my} - \frac{Dt}{m}$$

and

$$N_t = N_{(m-1)t/m} \cdot \left[1 + \frac{t}{m}\left(bp - \frac{1}{y}\right)\right] - \frac{Dt}{m}$$

Expressing N_t in terms of N_o, it can then be shown that:

$$N_t = \left[N_o - \frac{D}{bp - \frac{1}{y}}\right]\left[1 + \frac{t}{m}\left(bp - \frac{1}{y}\right)\right]^m + \frac{D}{bp - \frac{1}{y}}$$

In the limit, as the number of intervals $m \to \infty$ and each time interval $\to 0$,

$$\underset{m \to \infty}{Lt} \; N_t = \left[N_o - \frac{D}{bp - \frac{1}{y}}\right] \cdot e^{t\left(bp - \frac{1}{y}\right)} + \frac{D}{bp - \frac{1}{y}} \qquad \ldots\ldots\ldots(1)$$

where e is the exponential function.

7. Now let us examine the changes in the vaccinated section of the population. These changes in the number of vaccinated animals arise solely from deaths because it has been postulated that no vaccinations are given after time zero.

* More complicated expressions introducing the period of gestation and the risk of death during pregnancy are considered to be unnecessary refinements.

It will be assumed that the expectation of life of vaccinated animals is y years, as in the total population. An effective shooting campaign would attempt to concentrate on unvaccinated animals, but, for generality, let

d = number of vaccinated animals shot per year

and dt/m = number of vaccinated animals shot in any small interval of t/m years.

Let n_o = number of vaccinated animals at time o.

$n_{t/m}$ = number of vaccinated animals at time t/m, etc.

Then the number of vaccinated animals at the end of an interval = the number of animals at the beginning of the interval minus the number of deaths (normal and shooting) of vaccinated animals during the interval.

Hence $$n_{t/m} = n_o \left[1 - \frac{t}{my}\right]^{\frac{dt}{m}}$$

and $$n_{2t/m} = n_{t/m}.\left(1 - \frac{t}{my}\right) - \frac{dt}{m}$$

$$n_t = n_{(m-1)t/m}.\left(1 - \frac{t}{my}\right) - \frac{dt}{m}$$

Expressing n_t in terms of n_o it follows that

$$n_t = n_o\left(1 - \frac{t}{my}\right)^m + dy\left[\left(1 - \frac{t}{my}\right)^m - 1\right]$$

and in the limit as $m \to \infty$,

$$\operatorname{Lt}_{m \to \infty} n_t = n_o e^{-t/y} + dy\left(e^{-t/y} - 1\right) \quad \ldots (2)$$

The proportion of vaccinated animals at time 0 is

$$v_o = n_o/N_o$$

and the proportion after t years is

$$v_t = n_t/N_t$$

8. The equations (1) and (2) simplify in special cases. For example :

(i) If no animals are shot, then

$$D = d = 0$$

$$N_t = N_o.e^{t\left(bp - \frac{1}{y}\right)} \quad \ldots . (3)$$

$$n_t = n_o.e^{-t/y} \quad \ldots . (4)$$

$$v_t = v_o.e^{-tbp} \quad \ldots . (5)$$

(ii) If no vaccinated animals are shot, then

$$d = 0$$

$$N_t = \left(N_o - \frac{D}{bp - \frac{1}{y}}\right).e^{t\left(bp - \frac{1}{y}\right)} + \frac{D}{bp - \frac{1}{y}} \quad \ldots . (1)$$

$$n_t = n_o.e^{-t/y} \quad \ldots . (4)$$

9. In applying these formulae to estimate the vaccinated proportion, certain necessary conditions limiting the magnitudes of d and D must be observed. Clearly :

(i) n_t cannot be negative, hence

$$d \leq \frac{n_o e^{-t/y}}{y(1 - e^{-t/y})} \quad \ldots . (6)$$

(ii) N_t cannot be negative, that is

$$D \leqslant \frac{(bp - \frac{1}{y})\, N_0 e^{t(pb - \frac{1}{y})}}{e^{t(pb - \frac{1}{y})} - 1} \qquad \ldots\ (7)$$

and (iii) obviously,

$$n_t \leqslant N_t$$

10. *An alternative shooting scheme.*

Suppose that instead of shooting a fixed number of animals in each time interval, the shooting programme is defined in terms of fixed proportions as follows:—

Of the *unvaccinated* animals at the beginning of each interval of t/m years let a fixed proportion st/m be shot during the interval.

Of the *vaccinated* animals at the beginning of each interval let a fixed proportion s't/m be shot during the interval. The amount of shooting varies with the number of animals. For vaccinated animals

$$n_{t/m} = n_0 \left[1 - \tfrac{t}{m}(\tfrac{1}{y} + s')\right]$$

$$n_{2t/m} = n_{t/m} \cdot \left[1 - \tfrac{t}{m}(\tfrac{1}{y} + s')\right]$$

and $n_t = n_0 \left[1 - \tfrac{t}{m}(\tfrac{1}{y} + s')\right]^m$

When $m \to \infty$,

$$\operatorname*{Lt}_{m \to \infty} n_t = n_0 e^{-t(\frac{1}{y} + s')} \qquad \ldots\ (8)$$

For the total population:

$$N_{t/m} = N_0 + N_0 \tfrac{tbp}{m} - N_0 \tfrac{t}{my} - n_0 s' \tfrac{t}{m} - (N_0 - n_0)\tfrac{st}{m}$$

$$= N_0\left[1 + \tfrac{t}{m}(bp - \tfrac{1}{y} - s)\right] + n_0 \tfrac{t}{m}(s - s')$$

$$N_{2t/m} = N_{t/m}\left[1 + \tfrac{t}{m}(bp - \tfrac{1}{y} - s)\right] + n_{t/m} \cdot \tfrac{t}{m}(s - s')$$

and after m intervals,

$$N_t = N_{(m-1)t/m} \cdot \left[1 + \tfrac{t}{m}(bp - \tfrac{1}{y} - s)\right] + n_{(m-1)t/m} \tfrac{t}{m}(s - s')$$

Expressing N_t in terms of N_0, we obtain

$$N_t = N_0\left[1 + \tfrac{t}{m}(bp - \tfrac{1}{y} - s)\right]^m + \frac{n_0}{1 - \frac{bp}{s - s'}}\left[\left(1 - \tfrac{t}{m}(\tfrac{1}{y} + s')\right)^m - \left(1 + \tfrac{t}{m}(bp - \tfrac{1}{y} - s)\right)^m\right]$$

and as $m \to \infty$

$$\operatorname*{Lt}_{m \to \infty} N_t = N_0 e^{t(bp - \frac{1}{y} - s)} + \frac{n_0}{1 - \frac{bp}{s - s'}}\left[e^{-t(\frac{1}{y} + s')} - e^{t(bp - \frac{1}{y} - s)}\right] \qquad \ldots\ (9)$$

11. The total number of animals shot in the first t years is then

$$S_t = \tfrac{st}{m}\left[N_0 + N_{t/m} + \ldots\ldots\ldots\ldots + N_{(m-1)t/m}\right] - (s - s')\tfrac{t}{m}\cdot\left[n_0 + n_{t/m} + \ldots\ldots + n_{(m-1)t/m}\right]$$

and it can then be shown that

$$S_t/N_0 = \frac{s}{bp - \frac{1}{y} - s}\left(\frac{N_t}{N_0} - 1\right) + \frac{(s - s')(bp - \frac{1}{y})}{(\frac{1}{y} + s')(bp - \frac{1}{y} - s)}\left[\frac{n_t - n_0}{N_0}\right] \qquad \ldots(10)$$

12. The equations (8), (9), (10) simplify in special cases. For example:

(i) If no animals are shot, then

$$s = s' = 0$$

and $N_t = N_0 \cdot e^{t(bp - \frac{1}{y})}$ ..... (3)

$$n_t = n_0 \cdot e^{-t/y} \qquad \ldots\ldots\ldots (4)$$

$$v_t = v_0 \cdot e^{-tbp} \qquad \ldots\ldots\ldots (5)$$

$$S_t = 0$$

(ii) If no vaccinated animals are shot, then

$$s' = 0$$

$$N_t = N_0 \cdot e^{t(bp - \frac{1}{y} - s)} + \frac{n_0}{1 - \frac{bp}{s}}\left[e^{-t/y} - e^{t(bp - \frac{1}{y} - s)}\right] \qquad \ldots(11)$$

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$$n_t = n_o.e^{-t/y} \qquad \ldots\ldots\ldots (4)$$

$$S_t/N_o = \frac{s}{bp - \frac{1}{y} - s}\left[\frac{N_t - N_o + (bpy-1)(n_t - n_o)}{N_o}\right] \qquad \ldots\ldots\ldots(12)$$

(iii) If the shooting is indiscriminate so that vaccinated and unvaccinated animals are shot in equal proportion, then

$$s = s'$$

and $$N_t = N_o.e^{t(bp - \frac{1}{y} - s)} \qquad \ldots\ldots\ldots(13)$$

$$n_t = n_o.e^{-t(\frac{1}{y} + s)} \qquad \ldots\ldots\ldots(14)$$

$$v_t = v_o.e^{-tbp} \qquad \ldots\ldots\ldots(5)$$

and is independent of s.

$$S_t/N_o = \frac{s}{bp - \frac{1}{y} - s}\left(\frac{N_t}{N_o} - 1\right) \qquad \ldots\ldots\ldots(15)$$

(iv) If the maximum amount of shooting of all animals is carried out, then the proportion of vaccinated and unvaccinated animals shot in each time interval is unity.

i.e. $\frac{st}{m} = \frac{s't}{m} = 1.$

Then as $m \to \infty$

$$\text{Lt}\quad n_t = 0$$
$$\text{Lt}\quad N_t = 0$$
$$\text{Lt}\quad S_t = N_o$$

which is a complicated way of saying that all animals would be shot immediately.

Numerical examples.

13. It is roughly estimated for the dog population in Malaya that:

(i) the average expectation of life of an animal which survives the period shortly after birth is

$$y = 4 \text{ years},$$

(ii) the average number of viable pups produced annually per adult bitch is

$$b = 4 \text{ animals},$$

(iii) the proportion of bitches in the population is

$$p' = 1/6,$$

and defining an adult bitch as one aged 9 months or more, then the proportion of adult bitches in the population is assumed to be

$$p = p'\left(\frac{y - 3/4}{y}\right) = 13/96.$$

(iv) at time zero (January 1, 1955) the vaccinated proportion in Malaya was 0.9. That is

$$v_o = n_o/N_o = 0.9$$

We might also estimate the total population at time zero as $N_o = 100{,}000$, but in using the formulæ it is convenient to express the resulting estimates of N_t and S_t in terms of N_o without hazarding a numerical value for N_o.

14. Substituting these values of y, b, p and v_o, we can illustrate the formulæ with the following four examples. Examples 1 and 2 are concerned with the scheme in which the amount of shooting is fixed, and examples 3 and 4 with the alternative scheme in which the proportion shot is fixed.

Example 1.

15. A fixed number of animals, D, are shot each year but these include no vaccinated animals. That is, $d = o$. Then the number of vaccinated animals at time t is

$$n_t = n_o e^{-t/y} = 0.9\, N_o e^{-0.25t} \qquad \ldots\ldots (4)$$

and the total number of animals at time t is

$$N_t = \left[\left(1 - 3.425\, D/N_o\right) e^{0.292t} + 3.425\, D/N_o\right] N_o \qquad \ldots\ldots (1)$$

and the vaccinated proportion at time t is

$$v_t = n_t/N_t$$

In graph I, the vaccinated proportion v_t is plotted against time t for various values of D/N_o. Table I below summarises the corresponding values of N_t.

Table 1. Example 1. (No vaccinated animals shot.)

Number of animals, D, (all unvaccinated) shot per year, expressed as a fraction of N_o D/N_o	Total number of animals N_t, expressed as a fraction of N_o		
	after 1 year N_1/N_o	after 2 years N_2/N_o	after 3 years N_3/N_o
0	1.34	1.79	2.40
0.1	1.22	1.52	1,92
0.2	1.11	1.25	1.44
0.3	0.99	0.98	0.96
0.4	0.88	0.71	0.48
0.5	0.76		-

Thus, if no vaccinated or unvaccinated animals are shot, the vaccinated proportion v_t falls from the original 0.9 to 0.18 after three years (see graph I) and the total population rises to 2.4 N_o where N_o is the total population at time zero (see Table 1). To prevent the initial vaccinated proportion of 0.9 from falling below 0.7, the recommended safe proportion, it is necessary to shoot about $\frac{3}{8}$ N_o unvaccinated animals per year in the first three years—nearly 40,000 per year.

Example 2.

16. a fixed number, D, are shot each year, of which d are vaccinated animals. Then

$$N_t = 0.9\, N_o e^{-0.25t} + 4i\,(e^{-0.25t} - 1) \qquad \ldots\ldots (2)$$

and N_t remains the same as given in example 1.

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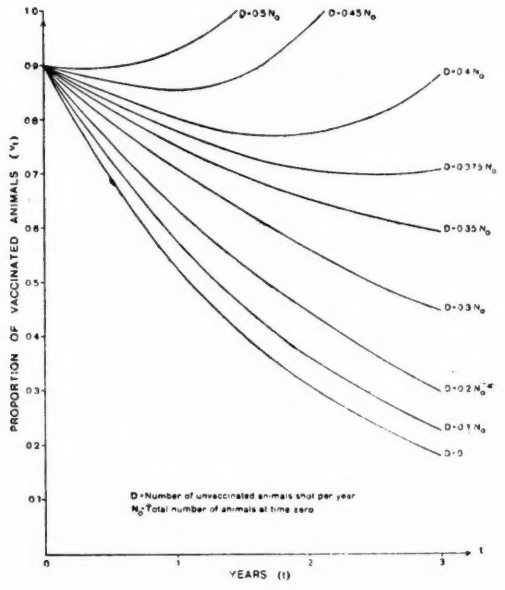
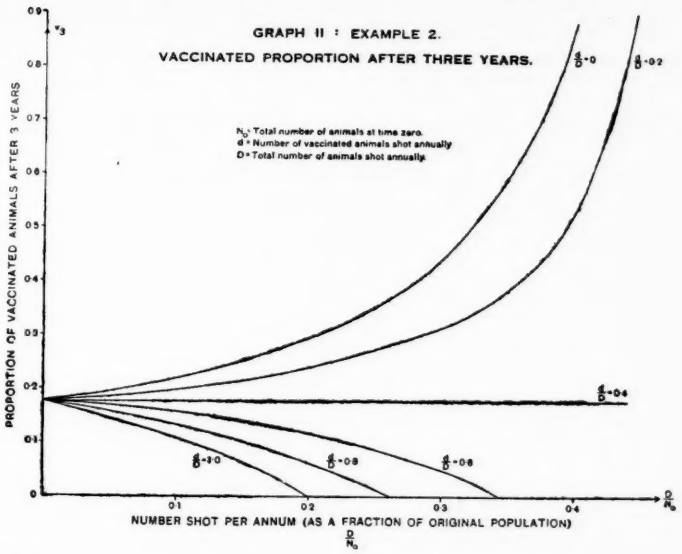
The vaccinated proportion after three years, v_3, is shown in graph II for various values of D/N_o and for different proportions of d/D.

We see from Graphs I or II that maintaining the vaccinated proportion after three years, v_3, above 0.7 requires the shooting of $\frac{3}{8}$ N_o animals per year when only *unvaccinated* animals are shot; but if the same total amount of

GRAPH I : EXAMPLE 1.
CHANGE IN PROPORTION VACCINATED
WHEN NO VACCINATED ANIMALS ARE SHOT



shooting includes 20 per cent vaccinated animals (i.e., $d/D = 0.2$) then the vaccinated proportion in the total population falls to about 0.45 after three years. If the shooting includes 40 per cent vaccinated animals ($d/D = 0.4$) then the vaccinated proportion v_3 falls to 0.18—which could have been achieved without any shooting. For values of d/D greater than 0.4, increased total shooting has an adverse effect on the vaccinated proportion after three years. Thus graph II demonstrates that the vaccinated proportion, v_t, cannot be maintained above 0.7 for three years without resorting to an extremely intensive shooting programme, and that even this would be ineffective unless the animals shot were either all unvaccinated or included merely a small proportion of vaccinated animals. Clearly, an indiscriminate shooting programme in which the chance of a vaccinated animal being shot was equal to that of an unvaccinated animal, would be doomed to failure.



Example 3.

17. No vaccinated animals are shot (i.e., $s' = 0$), but a fixed proportion, st/m of the unvaccinated animals is shot in each time interval of duration t/m. The equations become:—

$$n_t = 0.9\, N_0 . e^{-0.25t} \qquad \ldots\ldots\ldots\ldots\ldots\ldots (4)$$

$$N_t = \frac{N_0}{s - 0.542}\left[(0.1s - 0.542)e^{(0.292 - s)t} + 0.9s.e^{-0.25t}\right] \ldots\ldots (11)$$

and

$$S_t = \frac{s}{0.292 - s}\left[N_t - N_0 + 1.168\,(n_t - n_0)\right] \qquad \ldots\ldots\ldots (12)$$

$$v_t = n_t / N_t$$

In graph III, the vaccinated proportion v_t is shown plotted against time t for various values of s. These values of s do not provide an immediate indication of the amount of shooting, and so the corresponding values of S_t and N_t are given below in Table 2.

For example, if $s = 0.6$, $s' = 0$, the total number of animals shot in three years is $S_3 = 0.9\ N_0$ (i.e., about 90,000), the total population N_3 increases to $1.1\ N_0$, and the vaccinated proportion after 3 years is $v_3 = 0.39$ (see graph III).* Table 2 and graph III confirm that after three years without shooting the population rises to 2.4 times its original size and the vaccinated proportion falls from 0.9 to less than 0.2. Even when shooting is aimed solely at the unvaccinated

* In example 1, illustrating the case of shooting a fixed number of unvaccinated animals yearly, we find that for $d = 0$ and $D = 0.3N_0$ (corresponding to $S_3 = 0.9N_0$) the resulting N_3 value is $0.96N_0$, and v_3 is 0.44. The total number of animals shot in three years is equal in the two examples, but in the graph III case the number of animals shot in the third year is greater than in either of the previous years. Consequently, N_3 is greater and v_3 is smaller than for the case where the number shot per year is fixed.

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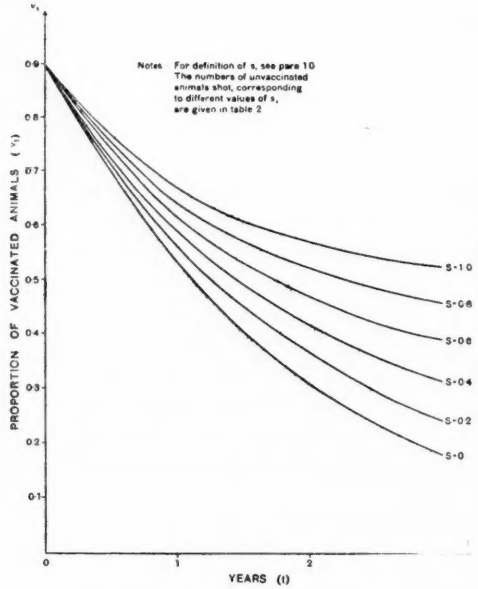
Table 2. Example 3. (No vaccinated animals shot.)

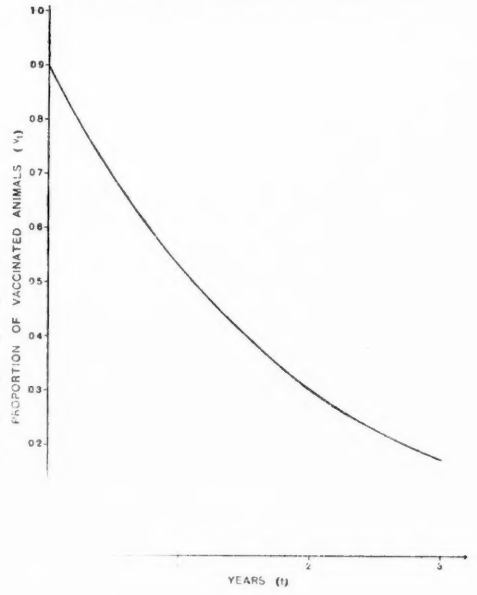
Fixed Proportion s	Total number of animals N_t, expressed as a fraction of N_0			Number of animals shot, S_t expressed as a fraction of N_0		
	After 1 year N_1/N_0	2 years N_2/N_0	3 years N_3/N_0	In 1 year S_1/N_0	2 years S_2/N_0	3 years S_3/N_0
0	1.34	1.79	2.40	0.0	0.0	0.0
0.2	1.26	1.52	1.76	0.07	0.22	0.45
0.4	1.20	1.31	1.36	0.12	0.38	0.73
0.6	1.14	1.16	1.10	0.17	0.49	0.90
0.8	1.10	1.05	0.93	0.22	0.58	0.99
1.0	1.06	0.96	0.81	0.25	0.64	1.05

and the total shot in three years amounts to the size of the original population (i.e., $S_3 = N_0$, and $s = 0.8$ approximately), yet the vaccinated proportion after three years, v_3, falls to less than 0.5.

GRAPH III : EXAMPLE 3.
CHANGE IN PROPORTION VACCINATED:
WHEN NO VACCINATED ANIMALS ARE SHOT.


Notes For definition of s, see para 10
The numbers of unvaccinated animals shot, corresponding to different values of s, are given in table 2
PROPORTION OF VACCINATED ANIMALS (v_t)
YEARS (t)
S-1·0
S-0·8
S-0·6
S-0·4
S-0·2
S-0

GRAPH IV : EXAMPLE 4.
CHANGE IN PROPORTION VACCINATED:
WHEN SHOOTING DOES NOT DISCRIMINATE
BETWEEN VACCINATED AND UNVACCINATED



Example 4.

18. Fixed proportions are shot without discriminating between vaccinated and unvaccinated animals,

Then $s = s'$

and $n_t = n_0 e^{-t(\frac{1}{y} + s)}$

$= 0.9N_0 e^{-t(0.25 + s)}$ .....(14)

$N_t = N_0 e^{t(bp - \frac{1}{y} - s)}$

$= N_0 e^{(0.292 - s)t}$ .....(13)

$v_t = v_0 . e^{-tpb}$

$= 0.9e^{-0.542t}$ .....(6)

$\frac{S_t}{N_0} = \frac{s}{0.292 - s}\left(\frac{N_t}{N_0} - 1\right)$ .....(15)

The vaccinated proportion v_t is shown in graph IV, and the values of S_t and N_t corresponding to different values of s when $s = s'$ are given in table 3.

Table 3. Example 4.
(Vaccinated and unvaccinated animals shot in equal proportion.)

Fixed proportion $s = s'$	Total number of animals N_t, expressed as a fraction of N_0			Number of animals shot S_t expressed as a fraction of N_0		
	After 1 year N_1/N_0	2 years N_2/N_0	3 years N_3/N_0	In 1 year S_1/N_0	2 years S_2/N_0	3 years S_3/N_0
0	1.34	1.79	2.40	0	0	0
0.2	1.10	1.20	1.32	0.21	0.44	0.69
0.4	0.90	0.81	0.72	0.38	0.72	1.03
0.6	0.74	0.54	0.40	0.52	0.90	1.18
0.8	0.60	0.36	0.22	0.63	1.00	1.23
1.0	0.49	0.24	0.12	0.72	1.07	1.24

The vaccinated proportion, v_t, is independent of the amount of shooting provided vaccinated and unvaccinated animals are shot in equal proportions. From its initial value of 0.9 at time zero, the vaccinated proportion falls to 0.5 after one year, 0.3 after two years, and 0.2 at the end of three years. This decline is the same as that encountered when there is no shooting.

Conclusions

19. These theoretical models emphasise the difficulty of maintaining a high proportion of vaccinated animals for a period of three years. It is estimated that, in the absence of shooting or further vaccinations, the proportion of immune animals undergoes a rapid decline. An indiscriminate shooting campaign which fails to concentrate heavily on unvaccinated animals will be equally ineffective. Even if the shooting can be restricted to unvaccinated animals, it is necessary to shoot an unrealistic number in order to control the fall in the immune proportion.

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20. It is recognised that the equations which have been derived are only a crude representation of the practical changes in the dog population, and precision cannot be claimed for the estimated parameters substituted in these equations in order to represent Malayan conditions. But the forecasts are considered sufficiently valid to justify a claim that a triennial vaccination campaign in Malaya will be too infrequent to maintain a high proportion of immune dogs.

Acknowledgments

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THE NUMBERS OF FAT GLOBULES IN THE MILK OF DISEASED COWS

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VARIATIONS in the percentage of fat of the milk yielded by normal cows are sometimes accompanied by changes in the size of the fat globules and occasionally there may be changes in the number of the globules. Collier (1891-2) examined successive pints from one milking and found a fairly steady increase in both the number and the relative size of fat globules from the first to the last pint and showed that these increases accompanied the increase in the percentage of fat. Woll (1894) found that when compared with the evening milk the higher percentage of fat in morning milk was accompanied by an increase in the size of the fat globules but that the number was the same for a given volume. Woll (1889-90) showed that the rise in percentage of fat which occurred as a lactation progressed was accounted for by an increase in the number of the globules in a certain volume of milk; the size of the globules declined towards the end of a lactation.

Observations were made on 20 cows which developed elevated body temperatures by King (1956), and he showed that a rise in body temperature was accompanied by a fall in yield and by increases in the percentage of fat and the average diameter of fat globules. Milk samples from 11 cows which did not develop a body temperature over 102.4° F. were collected on the second and seventh days after their admission to a veterinary hospital: when these were compared it was demonstrated that although on the seventh day there was a significant rise in the yield the differences in fat percentage and fat globule size were not significant.

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The work recorded here was undertaken to ascertain if changes in the percentage of fat of milk from similarly affected cows were accompanied by variations in the number of fat globules per unit volume.

Experimental Methods

All the figures given for yield, percentage of fat and numbers of fat globules are the averages of consecutive morning and evening milkings. The samples of milk were mixed thoroughly by rotating the bottles, but they were not agitated sufficiently to break the globules. The percentages of fat were determined by the B.S.S. No. 696 (1936) Gerber method and 1 ml. of milk was added to 9 ml. of water for counting the fat globules. One ml. of this mixture was added to 9 ml. of a mixture of equal quantities of glycerine and water. A drop of this was placed on a Thoma-Zeiss hæmocytometer slide, which was placed upside down for at least twenty minutes so that the globules rose and came in contact with the ruled scale. The slide was then turned the right way up and examined immediately. The globules in three large squares and two small ones (giving a total of 50 small squares) were counted, and the number of globules per cu. mm. calculated.

The rectal temperatures of the cows were taken before milking; from the results given in the literature (see King, 1955) it has been concluded that the temperature of a dairy cow at rest, unless taken immediately after feeding or milking, can rise to 102.4° F. before illness is suspected, but that a temperature of 102.5° F. or over suggests some abnormality.

The 27 cows from which milk samples were taken were all housed in loose-boxes while undergoing treatment at the University of Liverpool Veterinary Hospital in the period 1952-1956. Care was taken to see that factors, other than disease, known to affect the composition of milk did not have any influence on the samples examined. The cows were milked at the same time each morning and evening, and the milk was mixed thoroughly before samples were taken. The observations for each individual were made over a short period and therefore the advance in lactation would have little effect. A standard ration consisting of a proprietary brand of concentrates and hay was fed at all times, and samples were not taken from cows which were not eating. The cows from which the milk samples were examined were divided into two groups, those with "normal" and those with elevated body temperatures. Samples were not collected until the second day after an animal's admission to the Veterinary Hospital, to avoid the effect of travelling, or until five days after a Cæsarian Section operation had been performed; normal milk was then being produced. In those cows whose body temperatures were not raised, a second sample was taken five days after the first, and in those cows with raised body temperatures a second sample was taken when the temperature had returned to the normal range.

Results

Cows with "normal" body temperatures. Of the 17 cows which did not show a body temperature above 102.4° F., 12 were Friesians, three were

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Ayrshires, one was a Shorthorn and the other a Guernsey-Jersey cross. Ten had undergone Cæsarian Section operations, three had digits amputated, two had superficial abscesses, one had a rumenotomy operation and the other had been dehorned. The data from these are given in Table I.

TABLE I

The average milk yield, fat percentage and fat globule number per cu. mm. for the cows with "normal" body temperatures.

	(1) 1st day	(2) 5th day	Standard error of means
Average yield (lb.) ...	13.6	17.3*	± 1.5
Average fat content (%) ...	4.62	5.07*	± 0.17
Average fat globule number per cu. mm.	2,534	2,619	± 114

* The differences were significant at the 5 per cent level (i.e., the data analysed was sufficient to establish that in a series of 100 possible results, 95 would show that the effect did exist).

The milk yields were raised in 14 of the cows by the fifth day and remained unchanged in the other three. The percentages of fat were high in 14 cows, lowered in one and remained the same in the other two. The number of fat globules per cu. mm. was greater in nine cases and lower in eight. The increases in the yield and fat percentages were both significant at the five per cent level, but the fat globule number was not significant.

Cows with raised body temperatures. Samples were collected from 10 cows which developed body temperatures of 102.5* F. or over. Seven were Friesians and the other three were Ayrshires. Five had undergone Cæsarian Section operations, two had rumenotomy operations, one had an eye extirpated, one had metritis and the other acetonæmia. The data from these are given in Table II.

TABLE II

The average milk yield, fat percentage and fat globule number per cu. mm. for the cows with elevated body temperatures.

	Temperatures of 102.5° F. or over	Temperatures of 102.4° F. or under	Standard error of means
Average yield (lb.) ...	15.1	18*	± 0.7
Average fat content (%)	5.38	4.6*	± 0.22
Average fat globule number per cu. mm.	2,196	1,941	± 207

* The differences were significant at the 1 per cent level (i.e., the data analysed was sufficient to establish that in a series of 100 possible results, 99 would show that the effect did exist).

The fall in body temperature was accompanied by a rise in milk yield in all the 10 cows, and a drop in the percentage of fat in nine cases with a slight rise in the other. The number of fat globules per cu. mm. was lower in the "normal" temperature range in eight cases, and greater in the other two. The

rise in yield and fall in the percentage of fat were both significant at the one per cent level, but the difference in the fat globule number was not significant.

Discussion

The recovery of a cow from illness or from an operation in which there is an associated fall in body temperature may be accompanied by a rise in the milk yield. The fall in body temperature may also lead to a drop in the percentage of fat in the milk, whereas the recovery in cows which have not had an elevated body temperature may be accompanied by a significant rise. In neither case is there apparently a difference in the fat globule number per cu. mm. and therefore it appears that the variations in the fat percentages are not associated with changes in the number of fat globules per unit volume of milk.

Summary

The number of fat globules in a given volume of milk from 27 cows, which were in-patients in a veterinary hospital have been estimated. Seventeen of the cows did not develop a body temperature over 102.4° F., and samples were taken on two days with a five-day interval between. The other 10 cows developed raised body temperatures, and samples were taken when the temperatures were 102.5° F. or above and 102.4° F. or below. In both groups there was a significant rise in the yield of milk on recovery—in the cows with "normal" body temperatures it was significant at the five per cent level, and in the others at the one per cent level. A fall in body temperature was associated with a drop in the percentage of fat while recovery in the cows with "normal" body temperatures was accompanied by a rise in the fat. In neither group was the difference in the fat globule number per cu. mm. significant, and it appears that the variations in the percentages of fat are not associated with the changes in the number of fat globules per unit volume of milk.

My thanks are due to Professor J. G. Wright for allowing the work to be undertaken, to Mr. B. Burrows and other assistants at the Veterinary Hospital for taking the body temperatures of the cows and collecting the milk samples, and to Miss J. Ashcroft for assisting with the laboratory analyses.

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THE USE OF ŒSTROGENIC HORMONES AND HETEROGENEOUS SYNTHETIC SUBSTANCES WITH ŒSTROGENIC ACTION

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Œstrogenic Hormones

FEMALE sex hormones, œstradiol, œstron, œstriol and equilenin, hippulin and equilin discovered in the urine of mares are not single chemical compounds. In endocrinological terminology they are called œstrogenic hormones.

It appears that œstradiol is the true hormone (follicle-hormone or folliculesteron) while the others are probably different excretive forms with weaker biological effect. According to their chemical structure they belong to the steroid compounds (21, 31).

Œstrogenic hormones are formed in the female particularly in the ovarian follicles and in the placenta. They play an important role in the sexual cycle (2) and in pregnancy. Œstrogenic hormones are the progenators of secondary signs of sex and they are responsible for the periodicity of the sexual cycle. The general effects of these œstrogenic hormones have been known for a long time and physiologists have been able to indicate their specific actions. It has been established that they are not specific sex hormones because they are produced also in the male, particularly in the testicle. For instance, stallions excrete a considerable quantity of œstrogenic hormones, two and a half times more than the pregnant mare, and yet these males do not manifest the signs of feminism. Nature creates nothing without a definite purpose and it is supposed that these hormones in the male regulate the growth of the male sex organs (7). The fact that these hormones are found in the male and vice versa androgenous hormones in the female throws some doubt upon the nature of their sex specific actions. Investigations by biochemists, biologists, physiologists, clinical-workers and others have caused the previous ideas of the specific actions of œstrogenic and androgenous hormones to disappear; new pharmacological actions of œstrogenic hormones are being discovered (3). These hormones are not only sex hormones but they exert an influence upon the general metabolism (6, 12, 13, 17) of an organism. For that reason the œstrogenic hormones can be used with advantage in the treatment of many diseases.

Rowson *et al.* and other workers (1, 4, 10, 22, 23, 29, 30, 32, 38) have demonstrated that the endometrium is more resistant to infection in the œstrogenic phase. Heim, Koch and others confirm the possibility of strengthening the general resistance of the organism to infection by the aid of œstrogenic hormones. This may explain the higher percentage incidence of tuberculosis in working bullocks (on the Continent). Spörri suggested that castration is perhaps not so harmless to the health of animals as is generally thought.

There is no doubt that œstrogenic hormones can initiate or induce a variety of physiological and therapeutic effects (15, 16, 20, 34, 36, 39, 41, 53).

Some observations on the definition of Hormones and Hormonal-Therapy

It would be desirable to establish a more precise definition of hormone. This term should apply to those substances which possess specific actions, are products of endocrine glands and are transmitted from those glands into the blood stream.

One should try to avoid designating as a hormone each new compound discovered in the endocrine glands unless it can be proved to comply with the above definition. This is of special importance as regards the steroid-hormones of the adrenal cortex. About 30 steroids have been found which were all designated as hormones, whether they had or had not a biological effect. It was enough that these substances had been found in an endocrine gland. In this way confusion arises and renders more difficult further advances in endocrinological knowledge; we know that there are a smaller number of physiologically active hormones than the number of discovered steroids.

There is a pressing need to discontinue the practice of designating as hormones all those substances which are heterogeneous to the organism, but possess certain biological effects identical with those of the genuine hormones. For these substances the name pseudo-hormone is suggested. Just as the use of hormones in therapeutic practice is referred to as hormonal-therapy, so could the use of pseudo-hormone be referred to as pseudo-hormonal therapy. It is important also to bear in mind several facts which are of special importance for the rational adoption of hormonal-therapy and which are very often forgotten or are not given satisfactory attention when hormones are used for experimental or curative purposes.

Hormonal-therapy can be substitutive, equilibrous and symptomatic. As a rule and for economic reasons substitutive hormonal therapy is possible only in small animal practice. Hormonal-therapy demands an exact diagnosis and can be dangerous when diagnosis is incorrect (27, 28).

The second important factor concerns dosage. Hormones are biological products to which Arndt-Schultz's biological law can validly be applied. "A feeble stimulus incites; a medium advances; a strong hinders and a very strong stimulus breaks up the activity" (Schwache Reize die Lebenstätigkeit anregen, mittelstärke sie fördern starke sie hemmen und stärkste sie aufheben). This law was known also to Paracelsus, who said during his lifetime: "All substances are poisons and nothing is without poison; the dose alone decides whether a substance is a poison or not" (45). Doses of hormones are measured in standard international units. Small single doses which are usually ineffective will be effective when given several times (fraction dosage). In giving hormones in fraction dosages it is important to plan the interval between the doses; used in this way œstrogenic hormones develop their maximum effect if they are given at intervals of 6 to 8 hours. Shorter or longer intervals produce less effective action. This method of application is almost impossible for veterinary surgeons in country practices and probably could be used only in urgent obstetrical cases.

The next factor is the manner of administration. For example, thyroxine given orally has no influence on the blood sugar; given intravenously it increases it and when it is injected into the cerebral ventricle it decreases it. The solvent used and its rate of absorption is an important factor. Slow absorption is best. Absorption

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varies according to the species of animals to be treated. For instance, a comparative test of œstron dissolved in oil, alcohol and water was used to assess how many mouse units were equal to a rat unit; one rat unit of œstron dissolved in oil is equal to 36 mouse units; one rat unit of œstron dissolved in alcohol or water is equal only to 10 mouse units. This illustrates that hormones dissolved in oil have a stronger effect and probably a slower absorption rate and take longer to exert their effect than do hormones which are dissolved in alcohol or water. Veterinary surgeons often forget that there are different rates of absorption in the different species of animals.

The volume of the solvent is important also. Prolactin dissolved in 0.5 c.c. of the solvent has a stronger effect than the same quantity of prolactin dissolved in 0.05 c.c. of the same solvent.

External factors (food, management, movement, etc.) should not be forgotten when deciding whether to use hormonal-therapy or not.

Finally, it should be remembered that hormonal-therapy is not without danger. Hormonal-therapy demands of the persons who wish to use it a good knowledge of physiology (46, 47). Success is dependent upon a mature consideration of each individual case. Routine or mass therapy can bring discredit (28).

Heterogeneous synthetic Substances with Œstrogenic Action (Pseudo-œstrogens)

Dodd and his co-workers have isolated synthetic substances, the so-called stilbenes, which possess certain œstrogenic action (24, 33). These substances are chemically quite different from true œstrogenic hormones. The heterogeneous synthetic substances are very cheap but the cost of production of genuine œstrogenic hormones is very high. In veterinary practice the economic aspect of treatment is an important factor and it is not surprising that the use of synthetic substances with œstrogenic action has become popular. They have been used extensively and without previous controlled systematic research and it has led to many unexpected sequels. At the outset it was stated that differences existed between the biological effects of these substances and genuine œstrogenic hormones, but this was not emphasised sufficiently strongly. Products came into the hands of practitioners too early. In human medicine also, mass-use was made of these products. Clinicians were impressed by the prompt development of the external signs of œstrus after their administration. At that time Spörri said: "Genuine œstrogenic hormones should always be preferred to heterogeneous substances with identical effect." At first no one paid attention to this statement, which perhaps was given too guardedly. New synthetic substances continued to be discovered which had identical effects.

The products came into the hands of practitioners who had insufficient knowledge of endocrinology and the professional journals printed articles by several authors in which substances, which we now know are of problematic value, were pronounced a big success. These authors, when speaking of stilbenes and other heterogeneous synthetic substances with œstrogenic action, have used the terms—hormonal-therapy, hormonal castration, hormonal induction of lactation, hormonal interruption of broodiness, hormones inbreeding and animal production,

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hormonal fattening and hormonal sterilisation, etc. (5, 9, 11, 18, 19, 25, 26, 37, 41, 42, 48).

The general definition of hormones is known and it may be asked with reason why is the use of pseudo-œstrogens described under such titles? One may also ask, are these substances found in the ovarian follicles, or in the placenta or have we strayed from the true definition or enlarged upon it? The name synthetic œstrogens is not really satisfactory. In Switzerland a true syntheses of œstrogenic hormones has been successfully achieved but which is very expensive to produce and it does not lend itself to mass production. It remains but a scientific curiosity.

There are several hundred publications. A few analyse the use of œstrogenic hormones but a higher number describe the results with stilbenes and similar products in veterinary medicine.

In assessing dosage the use of the term international units (I.U.) has not been sufficiently stressed; it is very necessary that uniformity in terminology regarding dosage be achieved.

These are some of the reasons why hormonal-therapy has often been discredited and why a proper review of this subject has been impossible. Difficulties have been enhanced by many apparently contradictory publications.

From time to time the results of serious research have been published and among these were papers which brought to light new biological differences between œstrogenic hormones and pseudo-œstrogens, for example, the instability of dienœstrol and stilbœstrol (Smith, A. E., and Williams, P. C.), the toxicity of œstrogens (Nicol, T., and Hemmy, I. D.) and others (8, 43). The unwanted secondary effects are pointed out with increasing frequency and in consequence the use of these substances has diminished in human medicine. It has even been proposed that they should be excluded from use in medical practice (Varangot). Veterinary surgeons also began to use these products with caution. Analyses of practical results have been published in professional journals and would seem to indicate that care should be exercised in the use of these substances in veterinary gynæcology, especially in cases of ovarian insufficiency, but that they could be used with advantage in cases where it was desired to improve animal production. This means that the main uses of these substances were transferred from one field of treatment to another. A number of papers have been published which tell of the high concentration of these substances in meat and bacon and that in consequence these food products do not come up to the standard of hygiene required (Szumowski, Taylor) and others (14, 49). These facts are disputed by other authors.

Final Observations

The object of this article is to show that some progress has been made in our knowledge of endocrinology. Because new uses for œstrogenic hormones and pseudo-œstrogens have been found it is necessary to conduct systematic research and see if any biological differences exist between œstrogenic hormones and pseudo-œstrogens. It is not intended to imply that the use of pseudo-œstrogens should cease, but only that the further use of hormonal and pseudo-hormonal-therapy should be decided on the results ascertained by controlled experiments. Stilbœstrol or similar substances should not be classified under the term hormones.

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This is not merely a play on words but is a modest opinion that more confidence may be placed in the true hormonal-therapy which has suffered some discredit. Better co-operation between research workers and practitioners will perhaps indicate the precise value of genuine œstrogenic hormones in veterinary practice. An attempt has been made to indicate the complexity of the problem.

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INDIRECT BLOOD PRESSURE MEASUREMENT IN SHEEP AND GOATS EMPLOYING THE ELECTRONIC PLETHYSMOGRAPH: Validation against the Capacitance Manometer*

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Introduction

THE present study attempted to develop a valid and reliable indirect method of measuring blood pressure in sheep and goats.

It was found here that the auscultatory and oscillatory methods of measuring blood pressure cannot be applied to sheep and goats, although these methods provide satisfactory results in man and dogs. This is due in part to the difficulty in retaining a cuff in the correct position on a limb, and in part to the lack of a large superficial artery which provides a pulse of sufficient amplitude for application of either technique. In view of these facts another method was investigated. A modification of the Differential Impedance Recorder originally devised by Dubois and Nims (Noble, 1950*b*) has been used for the indirect measurement of blood pressure in rats (Noble, 1950*b*), and was found here also to provide satisfactory results in sheep and goats.

The Noble modification of the Electronic Plethysmograph was first used to measure systolic blood pressure in goats by Salpeter (1951). However, no correlation between the results of this method and direct blood pressure determinations was done at that time. Consequently, this study was concerned with comparing this method with an accurate direct method, the Capacitance Manometer (Noble, 1950*a*).

Apparatus and Method

The Electronic Plethysmograph (E.P.) provided a graphic representation of the pulse wave. This instrument measures the electrical impedance between two electrodes placed on the skin surface of a limb. Following the heart cycle the impedance between the two electrodes varies periodically due to a pulsing volume change in a given body segment. Changes in impedance registered as the pressure in the occluding cuff fell from above systolic to below diastolic blood pressure.

In the present experiment the apparatus and technique used by Noble (1950*b*) and Salpeter (1951) were modified. For our purpose the electrodes were applied to the metatarsal region. The electrodes assembly consisted of a bakelite block upon which two electrodes of thin metal plate were fixed 1½ inches apart.

Two different types of cuff were used, acccording to the size of the animals. One was the ordinary human-type blood-pressure cuff (9 x 17.5 cm.) and the other a larger, metal-ribbed, hook-type cuff (13 x 22 cm).‡

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‡ V. Muller & Co., Chicago, Illinois, U.S.A., General Catalog No. DS-556.

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The cuff was applied between the stifle joint and the tarsal region of the goat's leg. The internal or preferably the external part of the metatarsal region of the same leg was shaved and spread with Cambridge conducting jelly for application of the Electronic Plethysmograph electrodes. The electrodes assembly was attached rather lightly to prevent arterial occlusion. The pressure cuff was then slowly and smoothly inflated. The instrument records a straight line when arterial circulation is cut off. The cuff was then slowly deflated. When systolic pressure is reached small pulse-waves appear. The waves gradually increased in amplitude, reaching a maximum amplitude when the pressure in the cuff approached diastolic pressure. During deflation the pressure within the cuff was recorded directly on the tracing in 10 mm. Hg. intervals. Diastolic blood pressure was noted at the point at which the first wave of maximum amplitude appeared. This procedure was repeated several times on each experimental animal.

Using this method, measurements on a group of eight young unanæsthetised goats indicated a mean systolic pressure of 121.1 ± 10 mm. Hg. and a mean diastolic pressure of 79.5 ± 5 mm. Hg.

Since several investigators have claimed that any indirect method which involves the application of a cuff should be considered inexact, the following experiments were carried out to compare the measurements obtained by the use of the Electronic Plethysmograph (E.P.) with those obtained by an accurate direct method, the Capacitance Manometer (C.M.).

Experiments were performed on 16 goats and 4 sheep of various sizes and ages. The animals were anesthetized at a surgical level with pentobarbital sodium and placed on their backs with hind legs placed laterally, as horizontal as possible. In all cases it was found necessary to administer additional anæsthetic during the operation. The right leg was prepared for the needling of the femoral artery, which was exposed through an incision in the overlying skin and muscles. The blood-pressure cuff and the electrodes were applied to the left leg. In order to have the outputs of both the E.P. and the C.M. recorded simultaneously, a dual-channel Brush oscillograph was used. This allowed direct comparison of the results of both methods throughout the entire experimental session. The E.P. was adjusted according to the proper technique (Salpeter, 1951). The technique for the C.M. was the same as described by us in another work (Romagnoli, 1953). The records were examined for a comparison between the direct blood-pressure obtained from the right femoral artery 4 cm. below the inguinal ligament, and that simultaneously obtained by the E.P. from the left leg.

The goats and sheep employed were divided into groups according to size and weight.

I.—*Goats.*

(*a*) Eight young small goats weighing from 25 to 50 lb. were used for 10 experiments. In this group the small blood-pressure cuff (7 x 17 cm.) was applied in the femoral region of the thigh. Occluding pressure was therefore applied at the same level at which direct measurements were taken on the opposite leg.

(*b*) Four young goats of medium size (from 50 to 90 lb.) were used for five experiments. Because of the different sizes of the animals in this group, the cuff used was the same as that used in the first group, but it was applied below the knee between the stifle joint and the tarsal region of the leg.

(*c*) Four adult goats weighing over 90 lb. were used for five experiments In this group the cuff was also placed below the knee, but the larger hook-type cuff was used. This cuff was found to fit the larger legs of these animals better.

II.—*Sheep.*

(*a*) Two young medium-sized sheep weighing about 70 lb. were used in this group. Two different experiments ("A" and "B") were carried out on each animal. In the first experiment the ordinary cuff was applied in the femoral region. In this case the length of the cuff was roughly equal to or less than $1\frac{1}{2}$ times the diameter of the limb to which it was attached. In the second experiment the hook-type was applied between the stifle joint and the tarsal region. The length of the cuff in this case was always more than $1\frac{1}{2}$ times the diameter of the limb to which it was attached. Comparison of blood-pressure results obtained simultaneously by the E.P. and the C.M. was carried out in each group.

(*b*) Two adult sheep weighing over 100 lb. were used for five experiments. The large hook-type cuff was applied between the stifle joint and the tarsal region of the animal's leg.

Results

In the case of young goats (Group I [*a*]) the E.P. systolic pressure averaged 3.1 mm. Hg less than the value obtained from the C.M. (Table I). In the

TABLE I

Young Goats (Group I a)

Goats No	SYSTOLIC PRESSURE (mm Hg)			DIASTOLIC PRESSURE (mm Hg)		
	Capacitance Manometer	Electronic Plethysmograph	Difference	Capacitance Manometer	Electronic Plethysmograph	Difference
2	146.5	143.0	-3.5	99.5	95.2	-4.3
8	114.0	112.6	-1.4	74.0	81.6	+7.4
	124.0	119.0	-5.0	93.0	89.0	-4.0
9	126.2	125.7	-0.5	89.8	83.8	-6.0
17	131.4	127.2	-4.2	100.0	94.5	-5.5
24	135.1	132.6	-2.5	96.5	91.1	-5.4
25	120.3	110.3	-10.0	81.3	76.3	-5.0
	127.7	123.2	-4.5	98.7	89.7	-9.0
26	113.0	111.6	-1.4	88.0	79.5	-8.5
29	105.0	107.0	+2.0	69.5	69.0	-0.5
Mean	124.3	121.2	-3.1	89.0	84.9	-4.1

case of only one goat was the E.P. systolic pressure higher than the corresponding direct pressure. Concerning the diastolic pressures, the average discrepancies were about the same, but in most of the cases the E.P. method gave a lower value.

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With goats of medium size (Group I [*b*]), the E.P. systolic pressure obtained was slightly lower in three experiments and slightly higher in the remaining two. The E.P. diastolic was from 5.3 to 7 mm. Hg below the C.M. readings except in one case in which the E.P. diastolic was slightly higher than the C.M. reading by 2.3 mm. Hg (Table II).

TABLE II

Medium size goats (Group I b)

Goats N°	SYSTOLIC PRESSURE (mm Hg)			DIASTOLIC PRESSURE (mm Hg)		
	Capacitance Manometer	Electronic Plethysmograph	Difference	Capacitance Manometer	Electronic Plethysmograph	Difference
1	141.0	138.7	-2.3	97.2	90.7	-6.5
	133.0	134.5	+1 5	94.0	88.0	-6.0
4	151.0	145.2	-5.8	104.0	98.7	-5.3
5	132.0	134.3	+2.3	91.0	93.3	+2.3
23	150.0	148.0	-2.0	105.2	98.2	-7.0
Mean	141 4	140.1	-1.3	98.2	93.7	-4.5

In the case of large goats (Group I [*c*]), the systolic pressure obtained with the E.P. was lower than the C.M. reading in all but one case (Table III). In this group a fair agreement exists between the E.P. diastolic pressure and the C.M. diastolic pressure.

TABLE III

Adult Goats (Group I c)

Goats N°	SYSTOLIC PRESSURE (mm Hg)			DIASTOLIC PRESSURE (mm Hg)		
	Capacitance Manometer	Electronic Plethysmogaph	Difference	Capacitance Manometer	Electronic Plethysmograph	Difference
3	122.3	129.5	+7.2	85.3	91.0	+5.7
40	153.5	150.0	-3.5	99.0	95.5	-3.5
	149.4	146.6	-2.8	96.4	99.2	+2.8
178	136.0	131.8	-4.2	84.2	83.1	-1.1
90	141.7	136.2	-5.5	90.5	91.7	+1.2
Mean	140.5	138.8	-1.7	91.0	92.1	+1.1

In results obtained using the 9 x 17 cm. cuff with medium-size sheep (Table IV, Exp. "A"), the systolic pressure averaged 7.7 mm. Hg higher than the C.M. systolic pressure. The diastolic pressure measured with E.P. was about 7.0 mm. Hg higher than that of the direct method. However, the use of the larger hook-type cuff gave pressures more closely approximating to those obtained with the C.M. (Table IV, Exp. "B").

In adult sheep, E.P. systolic pressures were slightly below the C.M. pressure with the use of the hook-type cuff. On the other hand, the E.P. diastolic readings varied ± 2.6 mm. Hg when compared with the corresponding value obtained by direct arterial puncture (Table V).

Discussion

Pressures obtained by means of the E.P. on both young and medium goats (Group I and Group I [*b*]) showed a close correlation with direct arterial

puncture C.M. results. Although the average discrepancy was about the same for systolic and diastolic pressures, a wider range of variation was observed for diastolic.

In the majority of cases E.P. blood-pressure values are lower than corresponding C.M. values. The discrepancy between the methods is more marked in the case of adult goats than in the case of young and medium goats (Group I [*c*]).

TABLE IV

Medium size sheep (Group II a)

EXPERIMENT "A"

Sheep N°	SYSTOLIC PRESSURE (mm Hg)			DIASTOLIC PRESSURE (mm Hg)		
	Capacitance Manometer	Electronic Plethysmograph	Difference	Capacitance Manometer	Electronic Plethysmograph	Difference
31	124.0	130.0	+6.0	69.5	78.0	+8.5
34	133.6	142.8	+9.2	92.7	98.2	+5.5
Mean	128.6	136.4	+7.6	81.1	88.1	+7.0

EXPERIMENT "B"

Sheep N°	SYSTOLIC PRESSURE (mmHg)			DIASTOLIC PRESSURE (mm Hg)		
	Capacitance Manometer	Electronic Plethysmograph	Difference	Capacitance Manometer	Electronic Plethysmograph	Difference
31	120.4	120.1	-0.3	75.5	79.3	+3.8
34	130.6	135.5	+4.9	90.3	88.7	-1.6
Mean	125.5	127.8	+2.3	82.9	84.0	+1.1

In regard to all three groups of goats, it appears that the systolic pressure values given by the E.P. in most of our experiments (80 per cent) is slightly lower. In addition, even when the E.P. systolic pressure is higher, the discrepancy between the two methods is less than 10 mm. Hg.

TABLE V

Adult sheep (Group II b)

Sheep N°	SYSTOLIC PRESSURE (mm Hg)			DIASTOLIC PRESSURE (mm Hg)		
	Capacitance Manometer	Electronic Plethysmograph	Difference	Capacitance Manometer	Electronic Plethysmograph	Difference
29,a	124.3	123.7	-0.6	91.2	88.6	-2.6
29,b	115.8	113.8	-2.0	83.8	83.6	-0.2
36,a	111.3	103.5	-7.8	70.0	72.5	+2.5
36,b	109.3	104.6	-4.7	69.6	71.3	+1.7
36,c	118.7	113.7	-5.0	81.7	79.5	-2.2
Mean	115.8	111.8	-4.0	79.2	79.1	-0.1

With regard to diastolic pressure, the results are similar to those obtained for the systolic pressure. The E.P. diastolic pressure values are usually lower than C.M. values and in few cases in which a higher value was observed, the discrepancy was less than 10 mm. Hg.

The tests carried out on sheep demonstrate that the E.P. is capable of giving systolic and diastolic values averaging approximately $\pm$ 3 mm. Hg about the true intra-arterial pressure values measured with the C.M. These values were obtained with the use of a cuff (13 x 22 cm.) which completely encircled the

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limb and whose width was at least 50 per cent wider than the diameter of the limb portion to which it was applied.

The use of the smaller cuff (9 x 17.5 cm.), which did not completely fulfil these specifications, gave systolic and diastolic values which were greater than the true arterial pressure and the pressure obtained with the E.P. method using the larger cuff.

Summary

A method of measuring indirect blood-pressure in goats and sheep by means of the Electronic Plethysmograph has been validated against simultaneous values obtained with the Capacitance Manometer. The tests were performed on a number of goats and sheep differing in weight and size. Examination of the data obtained from all animals shows that Electronic Plethysmograph systolic and diastolic pressures values are in close agreement with those given by the Capacitance Manometer. In a majority of cases, the Electronic Plethysmograph readings are slightly lower than the results obtained by direct arterial puncture.

Thus it may be concluded that the Electronic Plethysmograph when applied in accordance with the described technique, is a sufficiently accurate method to be used in the measurement of the blood-pressure in sheep and goats, either for experimental or for clinical purposes.

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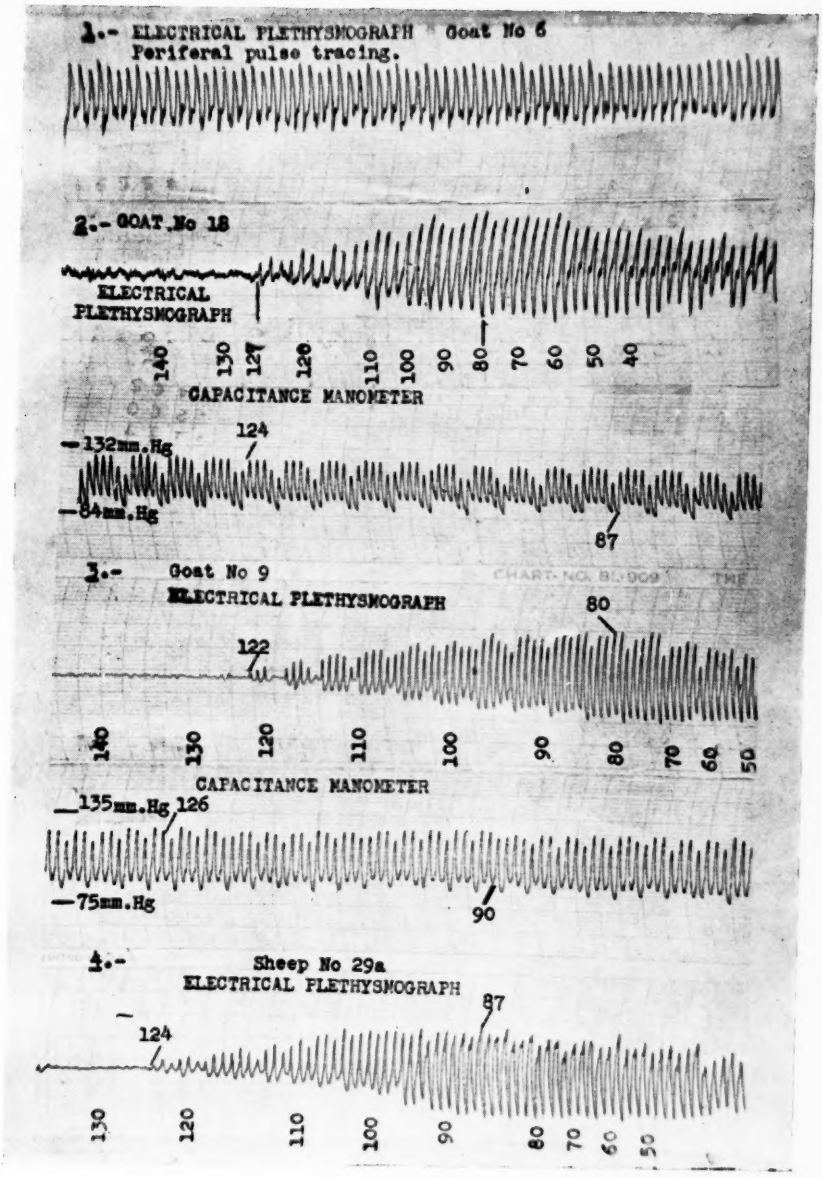

Fig. 1

Peripheral pulse tracing recorded by the Electronic Plethysmograph.
Blood-pressure measurement in goat (goat No. 18), Systolic 127 mm. Hg; Diastolic 80 mm. Hg.
Simultaneous recording of the blood-pressure with the C.M. and the E.P. in goat (goat No. 9), C.M. 124/87. E.P. 122/80.
Simultaneous recording of the blood-pressure with the C.M. and the E.P. in sheep (sheep No. 29), C.M. 126/90. E.P. 124/87.

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THE INCIDENCE OF AVIAN TUBERCULOSIS IN CHICKENS IN U.P. (INDIA)

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CHICKENS and many species of birds are susceptible to tuberculosis of the avian type and avian tuberculosis has been reported in mammals such as cattle, sheep, goats and the horse.

On rare occasions the avian tubercle bacillus has been found to be associated with tuberculosis in man. Evidence regarding the prevalence of tuberculosis in chickens in Indo-Pakistan is scanty. In view of the importance of tuberculosis it appeared desirable to inquire into the extent of its incidence in chickens in U.P. (India) in the period from 1942 to 1947.

Method and Materials

The birds were subjected to the intradermal tuberculin tests in the wattles. This was found to be the most dependable and practical means of detecting affected birds under field conditions. Flocks were tested periodically with avian tuberculin obtained from the Indian Veterinary Institute, Mukteswar.

A pronounced reaction persisting for 48 hours or longer was considered as positive, whereas the one fading away rapidly after 24 hours was regarded as doubtful. The birds reacting positively to avian turberculin were sacrificed for post-mortem examination. The lesions described here were those visible to the naked eye or with the aid of a lens and proved positive for acid-fast organisms.

Material from positive cases was sent to the Indian Veterinary Research Institute, Mukteswar, for typing. The organisms invariably proved to be of the avian type.

The first phase of the investigation included older farm-birds, two years of age or over, mostly of the exotic breeds. When a positive reactor appeared, the remaining birds in the flock irrespective of age were checked.

The second phase of the investigation included desi birds, mostly from the rural areas, as well as the randomly selected fowls assembled at the Government godowns for the supply to the Armed Forces stationed in India during the war. This represented a fairly representative sample of the indigenous fowls coming from all parts of the State.

The figures quoted here indicate the number of birds tested once only. The repeated testing at different intervals of the same flock was not considered toward counting the actual number of birds examined.

Summary and Results

The total number of fowls tested intradermally with avian tuberculin was 5,041 consisting of 1,338 birds of the exotic breeds and 3,703 desi fowls and some crossbred (desi and exotic). Out of 1,338 birds of the exotic breeds, 1,032 birds were from the urban areas concentrated on poultry farms. It was from this group

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that thirteen positive reactors (1.2 per cent) were detected and on post-mortem examination proved positive for acid-fast organisms. 306 birds raised in villages proved negative to these tests (Table I).

Table 1. showing the incidence of tuberculosis in exotic breeds of Chickens (U.P. INDIA).

(a) Birds kept on farms in Urban Areas.
(b) Birds raised in rural areas in small units.

	No. of farms or villages tested	Flock strength	Birds tested	Positive reactors	Doubtful reactors	Percent infection	REMARKS
(a)	10	1032	1032	13	2	1.2	
(b)	19 villages	306	306	Nil	Nil	Nil	
		1338	1338	13	2	0.9	

Out of 3,703 desi fowls and their crosses subjected to avian tuberculin tests (331 birds were from the urban areas) one positive reactor (W.L. x desi) was found. This bird came from a poultry farm where several tuberculous birds of the exotic breeds were found. The remaining 441 birds from 11 villages and 2,931 birds assembled at the Government godowns coming from various rural or urban parts of the State (U.P.) proved negative to the tests (Table 2).

Table 2. Incidence of tuberculosis in Desi-fowls (U.P. INDIA)

Birds from (a) Urban Areas (b) Rural Areas (c) Govt. Supply Godowns.

	No. of units or villages tested	Stocks strength	Birds tested	Positive reactors	Doubtful reactors	Percent infection	REMARKS
(a)	27	646	331	1 * (WL & Desi)	-	0.15	*From a farm having tuberculosis in exotic birds.
(b)	11	956	441	-	-	-	
(c)	-	*	2931	-	-	-	Random sample from hundreds of thousands of birds
			3703	1	-	Practically nil	

Tuberculosis in chickens has been reported to be an abdominal infection. The data contained in Table 3, showing the distribution of tuberculous lesions in various organs of the fowl indicated that liver (92 per cent) and spleen (77 per cent) showed lesions much more frequently than the intestines (54 per cent) though the infection in the latter was also fairly common. A large ulcer-like nodule imbedded in the structure of the proventricular wall having a calcareous deposit in the interior was observed in one fowl. Lesions in the proventriculus do not appear to have been reported before. No lesions of the disease were found in any other organs except one which was infected in the eye. The reaction of

this bird to avian tuberculin was considered to be anamolous until acid-fast organisms were demonstrated from the eye lesion.

No signs of any general disturbance was noticed following the injections of tuberculin intradermally and so far as it could be ascertained the birds appeared to be in the same condition during the reaction period as before or after.

Table 3. Distribution of lesions in the body of tuberculous fowls.

S. No.	Liver	Spleen	Intestines		Proventriculus	Eye	REMARKS
			Wall	Duod			
1	+	+	.	.	.	.	
2	+	+	.	.	.	.	
3	+	+	.	.	.	.	
4	+	+	.	.	.	.	
5	+	+	+	.	+1	.	1. A large nodular ulcer with calcareous deposit
6	+	+	+	.	.	.	
7	+	.	+	.	.	.	
8	+	+	+	.	.	.	
9	+	+	+	+2	.	.	2. Discharging ulcer.
10	.	.	.	.	.	-3	3. No visible lesions other than the ocular nodule having acid fast organisms.
11	+	+	.	.	.	.	
12	+	.	+	.	.	.	
13	+	+	.	.	.	.	Positive reaction to avian tuberculin
%	92%	77%	(46% 54%	*)	*	*	* Infrequent or rare
							+ = positive for tuberculosis

Conclusions

The epidemiological aspect of avian tuberculosis in chickens in U.P. (India) has been explored. In reviewing the evidence summarised above, it appears that avian tuberculosis is associated with over-population and congestion. The indigenous fowls usually kept in twos and fours were found to be free of the infection. Fowls of the exotic breeds kept in small units either in urban or rural areas were also found free of the disease.

In the present investigation the disease was found to be restricted in the main to the exotic birds concentrated on the farms. The liver and spleen were the organs more frequently affected.

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EFFECTIVE DRUGS FOR TREATMENT OF FAVUS IN POULTRY

By ALBERT LATIF, Ph.D., and HUSSIEN REDA, M.V.Sc.

Historical

Hutyra, Marek and Manninger (1938) used 10 per cent salicylic acid ointment, tincture of iodine diluted with 1 to 5 parts of alcohol, corrosive sublimate in spirit (0.5 per cent) in pyrogallic acid ointment for the treatment of favus in fowls. In addition, ointments containing carbolic acid (1 :20), calomel (1 :8) or creolin and painting the skin with 2 to 5 per cent formalin sol. or with benzine have been recommended. Rischmular (1937) treated cattle with derris 3 per cent Varenon (1941) treated infected horses by dressing them daily with 15-20 per cent alcoholic solution of salicylic acid and 20 per cent creolin ointment. Bryan and Young (1945) obtained good results by using phemoral in the treatment of infected calves.

Method and Technique

In this work 163 fowls of foreign and native breeds were used. Among the infected birds were 55 belonging to the flock of the Experimental Station of the Animal Nutrition Department, Faculty of Agriculture, Cairo University. The rest came from native farms.

The infection has been observed most frequently in foreign breeds and few cases were found in native fowls.

The crusts, taken from the favus lesions before the application of treatment, were examined microscopically for the presence of "Achorion Gallinæ." The lesions developed on the comb and wattles in the form of small, white patches resembling mould. In some cases the patches increased in number and size and finally coalesce to form a white coating covering the entire comb or wattle. In others, the deposit became gradually thicker and formed a wrinkled crust completely covering the comb and sometimes acquired a dark colour.

Therapeutics

The results obtained from treating scabies by the synthetic organic sulphur compounds induced us to use these products in the treatment of *Favus* a widely spread disease among poultry. The idea that biological activity in an organic compound is associated with particular chemical grouping present in its various modifications, and as the products obtained from the condensation of different aldehydes with hydrogen sulphide showed little activity towards the fungus causing the disease, our intention was drawn towards drugs containing the -SCN group. The latter group takes part in the molecule of many natural as well as synthetic active organic compounds (Murphy and Peet 1932; The Chemistry of Penicillin, Princeton Press, 1949).

As phenylthiocyanate showed better results, we tried to enhance its effect by the introduction of a negative group (like the nitro group) in different positions

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with respect to the thio cyanate group. Thus we prepared ortho-, para-, and meta nitrophenylthiocyanate and found that the ortho derivative had a great curative effect. Accordingly, o-dinitrophenylthiocyanate and sym-trimitrophenyl-thiocyanate were prepared. It was found that the action was enhanced by increasing the number of the nitro groups and reached its maximum effect with picrythiocyanate.

Preparation of phenythiocyanate

It was obtained by treating a suspension of potassium thiocyanate in dry benzene either with an equivalent amount of bromine (Kanfmann and Oehring, 1926) or with copper sulphate (Kanfmann and Kuchler, 1934).

$$2KSCN + Br_2 \longrightarrow 2KBr + (SCN)_2 \xrightarrow{C_6H_6} C_6H_5SCN + HSCN$$

$$2Cu(SCH)_2 + C_6H_6 \longrightarrow 2CuSCN + C_6H_5SCN + HSCN$$

It is mobile liquid b.p. 232 - 233° (corr.).

Para-nitrophenylthiocyanate

(Challenger and Collins, 1924) phenylthiocyanate (one mol.) was nitrates at 5-10° in the usual manner with a mixture of nitric acid (d.141) and sulphuric acid (d184) (1 : 1.5), a yellow solid was formed and the mixture was poured on ice. The solid was crystallised from alcohol when p-nitrophenylthiocyanate m.p. 133° was isolated (Z.).

Diazotization of nitroanilines

(Korcozynski, Schonlan and Fichter, 1915). This method was used for the preparation of O,p and m-nitrophenylthiocyanate and also for the preparation of o-dinitre and picryl thiocyanate from the corresponding nitre anilines as follows :—

The diazotised nitre aniline (one mol.) was treated with potassium thiocyanate (three mols.) and cobalt chloride (one mol.), taken with etherbenzene and then crystallised from alcohol.

o - nitre phenylthiocyanate	m.p. 132.5°
p - „ „ „	m.p. 133°
m - „ „ „	m.p. 56°
o - dinitre phenyl-thio-cyanate	m.p. 162°
picryl-thio-cyanate	m.p. 222°

Treating substituted chlorobenzene with ammonium thiocyanate

This method is used for the preparation of o-dinitrethiocyanate and picryl thiocyanate from o-dinitro-and sym-trinitre-chlorobenzene respectively. The chlorobenzene (one mol.) is added in portions to a diluted solution of ammonium thiocyanate (1.5 mol.) and heated at 50° for four hours and crystallised. (F.I.A.T., Final Report No. 949).

Treatment

Treatment is based on the application of drugs which have an effect on the favus without causing any harm to the host itself.

The infected birds were isolated. The crusts were softened with oil, then

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scraped and washed with warm water and soap. The infected parts in the comb and wattles were rubbed first with a solution of 10 per cent alcoholic hydrochloric acid (for the first five drugs) or a 5 per cent solution of chromic acid anhydride in acetic acid (10 per cent) (for the rest of the drugs; see accompanied table) and left to dry for ten minutes, These were afterwards rubbed with a 10 per cent oily solution of the drug. The lesions were scraped and well washed before each dressing. Scrapings were examined during treatment. The dressings were carried out every three days until scrapings were negative to favus. Most of the infected cases took from 5-6 dressings for complete recovery.

The results obtained are shown in the accompanied table.

The effect of different drugs on infected fowls

	Name of the drug	Total No.	No. cured	Percentage
1.	Thio-acetaldehyde	10	2	20.0
2.	Thio-acetaldehyde	12	3	25.0
3.	Thio-benzaldehyde	8	1	12.5
4.	Thio-benzaldehyde	10	2	20.0
5.	Thio-chloral	10	3	30.0
6.	Phenyl thiocyanate	15	5	33·3
7.	m-nitrophenyl thiocyanate ...	15	6	40.0
8.	p-nitrophenyl thiocyanate	13	6	46.2
9.	o-nitrophenyl thiocyanate	15	7	46.7
10.	o-dinitrophenyl thiocyanate ...	15	9	60.0
11.	Sym-trinitrophenyl thiocyanate (picryl thiocyanate) ...	28	28	100.0
12.	Picryl chloride	12	3	25.0

Discussion

The experiments proved that trinitrophenyl-thiocyanate is 100 per cent effective in the treatment of favus in fowls.

Summary

(1) Thioaldehydes, phenylthiocyanate, mono-, di- and tri-nitrophenyl-thiocyanate were used for treatment of favus in fowls.

(2) All showed various results on curing the infection.

(3) Picryl thiocyanate was the most effective drug.

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REVIEW

VETERINARY OPHTHALMOLOGY, by R. H. Smythe, M.R.C.V.S. London: Baillière, Tindall & Cox. Price, 35s.

NICOLAS published his book on Veterinary Ophthalmology many years ago and it was made available to the world by Henry Gray, who, being no mean scholar and a competent veterinary ophthalmologist, translated it into the English language. In human medicine, ophthalmology is very specialised and it is practised by those who can devote their whole attention to the subject. Members of other branches of the profession do not attempt to deal with serious affections of the eye and are content and indeed happy to refer cases to the ophthalmic surgeons. In veterinary medicine, mainly for economic reasons, specialist services are not available to the same extent and practitioners have to rely on their own skill and knowledge. In some ways this is good and it can be said with truth that the average practising veterinary surgeon has a more comprehensive knowledge of the surgical and medical affections of the eye than his medical colleague. Many practising veterinary surgeons can deal expertly with lesions of the eye which in human practice would be referred to a specialist ophthalmologist. The author of this book is recognised by his fellows as a clinician of high repute. One of the things which has attracted his attention is the eye and its appendages and it is not surprising that he has found the time to complete this erudite tome which represents a wide gleaning of the relevant literature and his own observations. The book is in two parts. In the first he has delved into the realms of comparative anatomy and physiology and discusses the structure and function of the eye in a variety of animals. He discusses the vagaries of animal vision, the optical system and accommodation. This method of introduction to the subject will come as no surprise to those who know the author, for one cannot imagine that he would proceed to the clinical dissertations without building upon a sound factual and, if one may say so, philosophical foundation. These chapters are of great interest and value. The clinical section deals with the more prosaic matters with which the practitioner is confronted in his daily work. The surgical and medical procedures necessary to alleviate and resolve the great variety of abnormalities, injuries and disease to which the eye is subject are discussed and illustrated with a lucidness which is impressive. All facets of veterinary ophthalmology are reviewed and, whilst not discarding those measures which have stood the test of time, the author places before his readers most valuable and up-to-date information regarding modern ophthalmology. In his final chapter therapeutics come under review. Again this is an epitome of the old and the new and he brings the discussion up-to-date by including modern antibiotic and hormone therapy. Many veterinary surgeons will find the list of prescriptions particularly useful. The book is replete with illustrations, line drawings, micro photos and photographs. It is a book that all veterinary surgeons and students should study. They may not agree with the author entirely, but their knowledge of veterinary ophthalmology will be enhanced, their interest in the subject will be aroused, and they will want more.

XUM

NEWS

International Congress on Animal Reproduction, 1956

THE third I.C.A. Reproduction will be held at Cambridge from June 25 to 30. We have received the provisional programme and it would appear that every possible facet of this intriguing topic will be covered. The list of speakers is truly international and all are recognised authorities in their particular specialties.

There are Plenary Sessions and Sectional Sessions. The Plenary papers cover Physiology, Pre-natal life, Genital Infection, The Effect of very low temperatures on cells and tissues, Advances in A.I. Techniques, and Nutrition in relation to reproduction.

The Sectional programme is replete with over one hundred papers which are of great variety. In addition there are exhibitions, demonstrations and films.

Those who attend this congress will have no cause to grumble about any shortage of intellectual food. It may be that it is so crowded with papers, demonstrations, etc., as to provoke a mental dyspepsia.

As in all well-organised congresses, the social side has not been forgotten, and no doubt if the members can spare the time from their more erudite pursuits they will enjoy the time they spent in Cambridgeshire..

Dr. Joseph Edwards is Hon. Secretary and Treasurer and no doubt further information could be obtained from him at The Milk Marketing Board, Thames Ditton, Surrey.

IMPERIAL CHEMICAL (PHARMACEUTICALS) LIMITED have now introduced "Phenovis" Phenothiazine Tablets (Mineralised). These tablets each contain 5 grammes of "Phenovis" Phenothiazine, together with the appropriate amounts of trace elements, copper and cobalt. They are additional to the "Phenovis" Mineralised Dispersible Powder which is already available for the treatment of roundworms in farm animals.

Retail Price: Packs of 50, 9s. each; Packs of 250, 40s. each.

ERRATUM

Article by R. N. Smith, page 176, May, 1956, third paragraph: Line two should read "was found that 11 had both metacarpals in both limbs and . . ."

Publishers' Notices

THE BRITISH VETERINARY JOURNAL, with which is incorporated THE VETERINARY JOURNAL, is published monthly, and copy for advertisements should be in the hands of the advertisement manager not later than the 20th of the preceding month, if proof is required. Tel.: Temple Bar 3386.

Letters for the Journal, literary contributions, reports, notices, books for review, exchanges, new instruments or materials, and all matter for publication (except advertisements) should be addressed to the Editor.

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